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RADIUM

EDITED BY

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AND

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VOL. I, New Series APRIL, 1922 No. 1

CONTENTS

Announcement 1
Radium Treatment of Carcinoma of the Bladder. Benjamin S. Barringer, M. D. 2
Carcinoma of Prostate. B. S. Barringer, M. D. 19
The Treatment of Carcinoma of the Prostate. John H. Cunningham, M. D. 32
Method for the Introduction of Radium Needles Into Tumors of the Bladder. John H. Cunningham, M. D. 40
Technique of Radium Treatment of Cancer of the Prostate and Seminal Vesicles. Hugh H. Young, M. D. 43
Results in One Hundred Cases of Cancer of Prostate and Seminal Vesicles, Treated With Radium. Clyde L. Deming, M. D. 52
Treatment of Malignant Disease of the Prostate and Bladder. J. T. Geraghty, M. D. 82
The Cystoscopic Application of Radium. Leo Buerger, M. D. 99
Radium in Cancer of the Bladder. George Gilbert Smith, M. D. 102

REVIEWS AND ABSTRACTS

Douglas Quick, M.D. The Treatment of Cancer of the Rectum by Radium 109

A QUARTERLY JOURNAL DEVOTED TO THE CHEMISTRY, PHYSICS AND THERAPEUTICS OF RADIUM AND RADIO-ACTIVE SUBSTANCES

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RADIUM

A QUARTERLY JOURNAL DEVOTED TO THE CHEMISTRY, PHYSICS AND THERAPEUTICS OF RADIUM AND RADIO-ACTIVE SUBSTANCES

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Edited by Charles H. Viol, Ph. D., and William H. Cameron, M. D., with the assistance of collaborators working in the fields of Radiochemistry, Radioactivity and Radiumtherapy.

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VOL. I, New Series APRIL, 1922 No. 1

ANNOUNCEMENT.

Beginning with this issue, RADIUM will appear in an increased size as a quarterly publication. During the past nine years RADIUM has been the means of disseminating information regarding the therapeutic uses of radium by presenting original articles and more particularly by reprinting in full and in abstract the best articles which appeared in the world's medical literature.

In 1913 when RADIUM was first issued, the literature of radiumtherapy was meager and largely European, while work in this field was greatly hampered by the lack of radium and suitable standards. With the general adoption of the International Gamma Ray Radium Standard since 1912, and with the production of radium on the largest scale in the United States since 1913, and by reason of the suspension of interest in radiumtherapy abroad during the period of the war, America has taken a lead in the therapeutic use of radium which it will probably always maintain. The result has been that our own medical journals now present the most authoritative articles on radiumtherapy.

In changing from a monthly to a quarterly publication, it will continue to be the policy of the editors to present to the readers of RADIUM, articles which represent the best work in the field of radiumtherapy and in the allied branches of physics and chemistry as far as they have a bearing in the therapeutic use of radium. The Editors.

RADIUM TREATMENT OF CARCINOMA OF THE BLADDER*

By BENJAMIN S. BARRINGER, M. D.
of New York

Clinical Report from the Memorial Hospital of New York

The treatment of carcinoma of the bladder at the Memorial Hospital has been divided into two periods, viz., that prior to June, 1919, when we were testing what could be done with radium applied through the urethra and without opening up the bladder; and that period since June, 1919, when we have added to the intraurethral treatment the application of radium through the bladder opened suprapubically. The object of this latter phase was to destroy extensive bladder carcinomata which we had not been able to cope with through the urethra. The results of both these forms of treatment are herein reported and this paper is based upon all cases seen at the Memorial Hospital up to January, 1921, a period of nearly five and a half years. One hundred and forty-two cases of advanced carcinoma; four cases of small carcinoma; nine cases of extensive papilloma; two borderline cases.

Pathology—Classification.—In fifty-three cases of tumor of the bladder the pathological examination (Ewing) was as follows: Papilloma, seven cases; papillary carcinoma, eighteen cases; infiltrating carcinoma (variously called epidermoid carcinoma, malignant epithelioma, papillary infiltrating carcinoma), twenty-two cases; adenocarcinoma of prostatic type (alveolar carcinoma), four case; papillary adenocarcinoma, one case.

I can see no reason for making another class "malignant papilloma," which means that a tumor purely papillomatous in histological structure, either by its rapid growth or rapid recurrence after removal, shows more malignant tendencies than the usual papilloma. The term "malignant papilloma" refers to a clinical rather than a histological difference. In these fifty-two cases there was but one which could not be classified under the above heading, that of papillary adenocarcinoma. The four cases of alveolar carcinoma were probably secondary to a prostatic carcinoma.

Papillary Degeneration into Carcinoma.—There has been much written over the fact that papillomatas may remain such for a long period and then take on a carcinomatous degeneration (Mandlebaum, the Pathology of New Growths of the Bladder; Surgery, Gynecology and Obstetrics, September, 1907; Buerger, Trans. of A. U. A., 1915). The basis for this rests upon two findings:

1. Clinical: A pure bladder papilloma may be observed at one time (cystoscopically and by pathological specimen), and a number of years later a well-developed carcinoma identified.

2. Pathological: The fact that a tumor shows in one part pure papilloma and in another part carcinoma may indicate that a benign papilloma has become carcinomatous.

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We have seen patients with extensive papillomata of the bladder with histories dating back four, five, six years and more which showed at the time of examination no malignant changes (pathological examination, Ewing), and which had no induration at the base of any of the multiple tumors. We have also seen patients with carcinoma of the bladder (identified pathologically and cystoscopically) live for a number of years with their carcinomas. Our observations lead us to believe that many bladder tumors run true to their original histological structure. Many papillomata begin and end papillomata, and many carcinomas begin and end as such. We must, however, not forget that malignant degeneration may take place in a papilloma and therefore papillomata are potentially malignant.

History.—Age first seen—125 cases (121 extensive carcinoma, four small carcinoma). Twenty to thirty years, three cases; thirty to forty years, sixteen cases; forty to fifty years, twenty cases; fifty to sixty

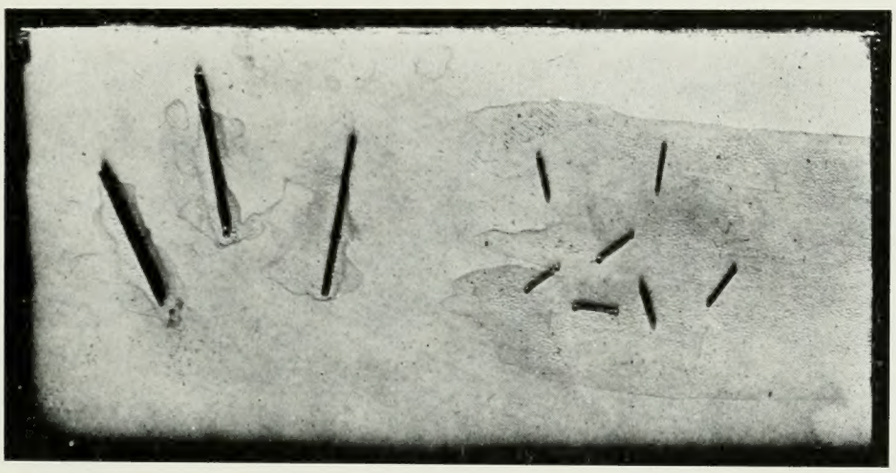

Fig. 1.—Tubes of radium emanation. The small tubes to right are "bare tubes" used to implant directly into tumors.

years, thirty-seven cases; sixty to seventy years, thirty-five cases; seventy to eighty years, fourteen cases.

The sixth and seventh decades showed the greatest incidence of carcinoma. Nine extensive papillomata of the bladder gave four cases between fifty and sixty; two cases between sixty and seventy; one case between seventy and eighty. So giving about the same age incidence as carcinoma.

Duration of Symptoms.—One hundred and twenty-one cases (116 advanced, five early carcinoma). One to three months, fifteen cases; three to six months, fourteen cases; six to twelve months, thirty-five cases; twelve to eighteen months, nine cases; eighteen to twenty-four months, sixteen cases; twenty-four months, 32 cases.

These tables emphasize that most patients with carcinoma of the bladder have symptoms for a year or more before their condition is seriously considered. If they could be seen earlier very many more could be cured.

Among the cases of extensive papilloma was one with symptoms dating back six years; he had extensive solid papillomata almost filling the bladder. There was no induration of the base of any of these; path-

ological examination (Ewing) showed papilloma. One extensive carcinoma of the bladder had bladder symptoms dating back fourteen years.

Sex.—On hundred and fifty-three cases—male, 119; female, 34. This preponderance of males may signify that inflammation may be a causative factor in carcinoma of the bladder. Prostatitis and trigonitis (gonorrhœal) have no analogue in the female.

Loss of Weight and Strength.—Of 126 cases (124 advanced carcinoma), thirty-nine cases showed a decided loss of weight. Loss of both weight and strength is commonly supposed to be an accompaniment of malignant disease. These two as a symptom of bladder carcinoma, generally appear late. In our records there are a good many cases of bladder

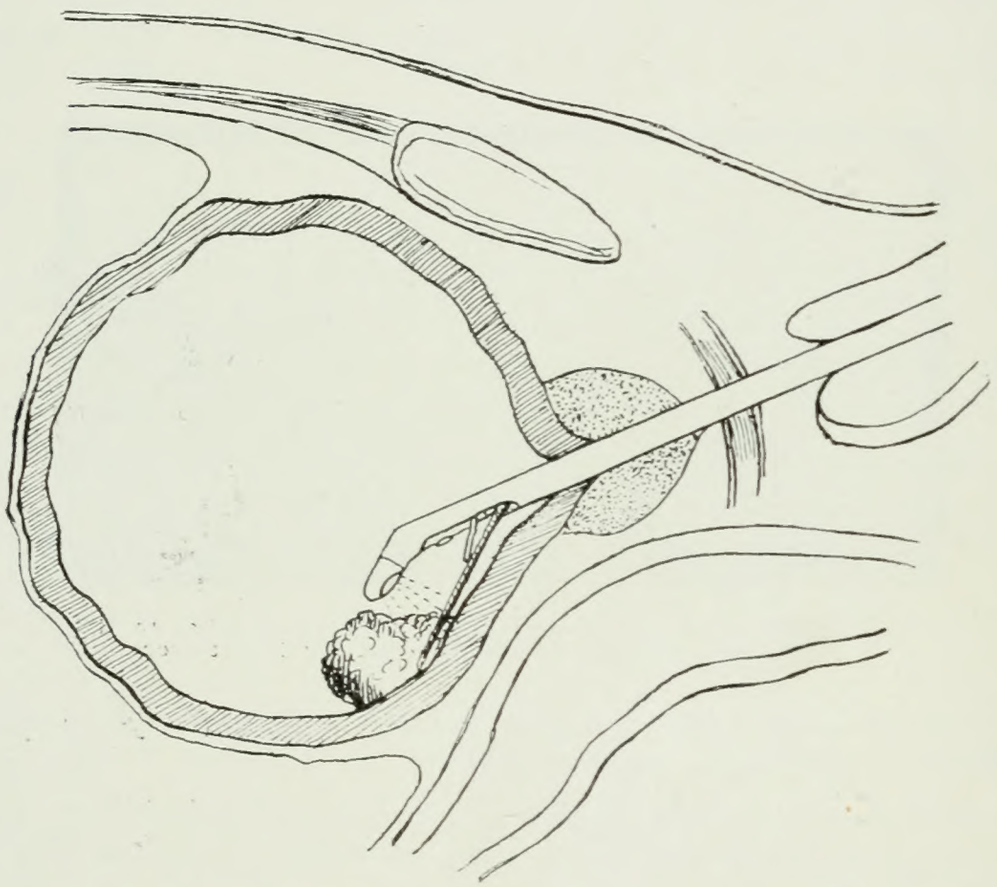

Fig. 2.—Method of burying radium emanation tubes in growth by means of special introducer and the cystoscope.

carcinoma too advanced for any therapy, which have kept both their weight and strength up to the time when seen. If the loss of weight be due directly to the carcinoma and not secondary as e. g., serious infection of the kidneys, then one may suspect that the carcinoma has grown beyond the bladder.

First and Second Symptoms.—One hundred and thirty-eight cases (135 advanced carcinoma, three small carcinoma).

Haematuria.—First symptom, seventy cases; second symptom, sixty cases; no hæmaturia, eight cases. This symptom of tumor of the bladder therefore appeared in 130 out of 138 cases. In recognizing this as a cardinal symptom in early cystoscopy and appropriate treatment thereafter lies the solving of the question of carcinoma of the bladder.

In eight extensive papillomas of the bladder, but one gave no history of hæmaturia.

Disturbance of Urination.—One hundred and eighteen cases (116 advanced carcinoma, two small carcinoma); first symptom, fifty-eight cases; second symptom, fifty-two cases.

The carcinoma in the majority of cases causes some urinary disturbance. Frequent urination, dysuria, polyuria, retention, incontinence.

Loss of Weight (116 cases).—First symptom, no cases; second symptom three cases.

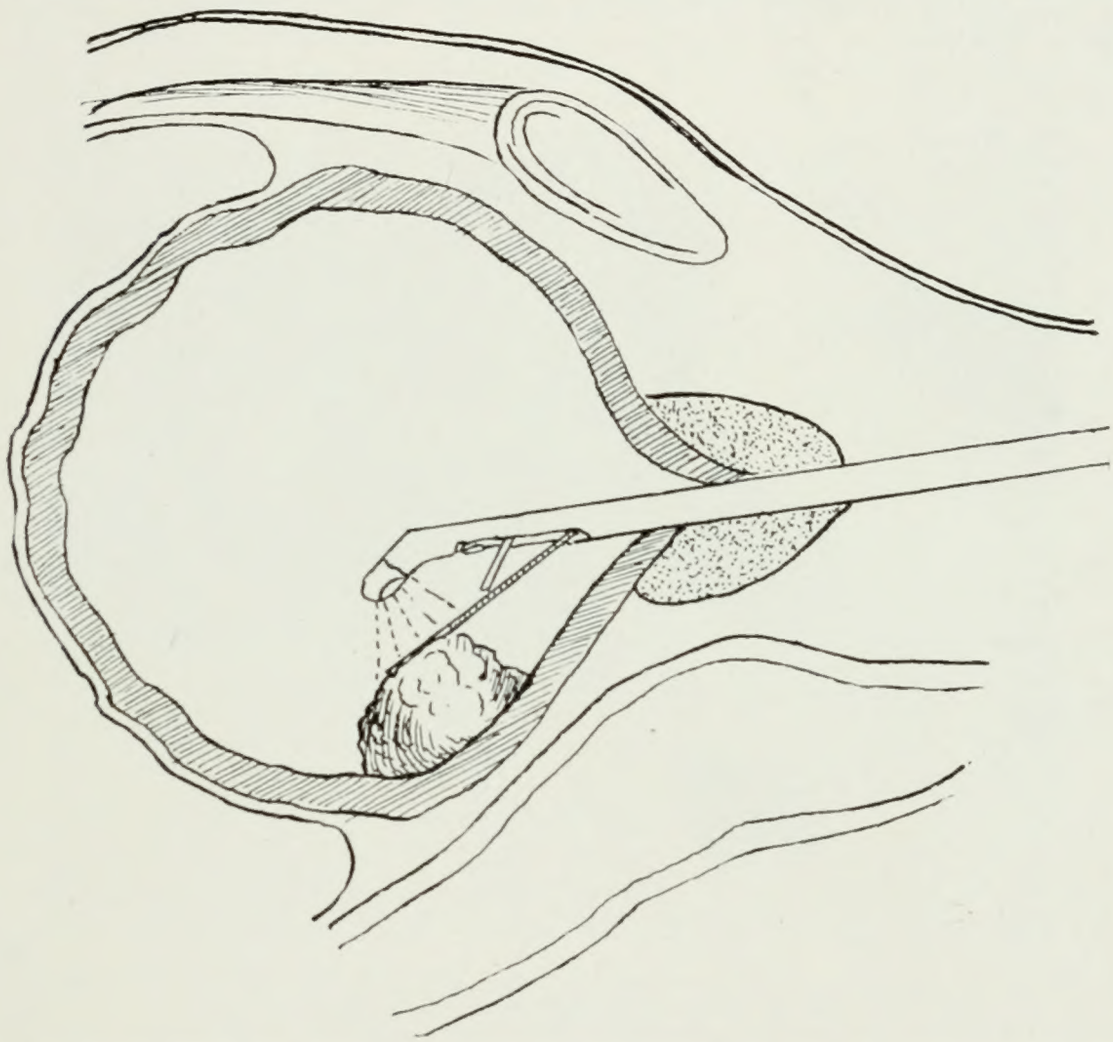

Fig. 3.—Surface application of radium emanation to growth under vision by means of special applicator in cystoscope.

This symptom so often seen in prostatic carcinoma is comparatively rare in bladder carcinoma and is almost always an index of nerve involvement by the carcinoma beyond the bladder.

EXAMINATION.—*Cystoscopy*: 1. Presence of Tumor. 2. Carcinoma or Papilloma. Usually the cystoscopic diagonsis is not difficult. If there is fresh bleeding, the best view of the bladder and tumor is made during irrigation. The red, fluffy papilloma may be confused with blood clots, and the gray, sloughy carcinoma with calcareous incrustation of the bladder. The examination of pieces of tumor obtained with the rongeur forceps (cystoscopic) or sticking to the cystoscope may confirm the diagnosis. Pieces of the white, sloughy portions of a tumor usually show nothing diagnostic microscopically.

Carcinoma or Papilloma.—It probably falls to our lot at the Memorial Hospital to see more carcinoma than papilloma. In five years we have seen very few, not more than five or six, papillomas which have been suitable for destruction by fulguration.* We have also seen many patients whose tumor has been fulgurated at length and often before they came to us with fullblown carcinoma. Extensive tumors of the red papillary type should be suspected of being carcinomatous, notwithstanding the oft-returning pathological report "papilloma." The more a tumor tends towards the flat type, the more malignant is it.

A raised thickened base means carcinoma. All sloughy tumors are carcinomatous.

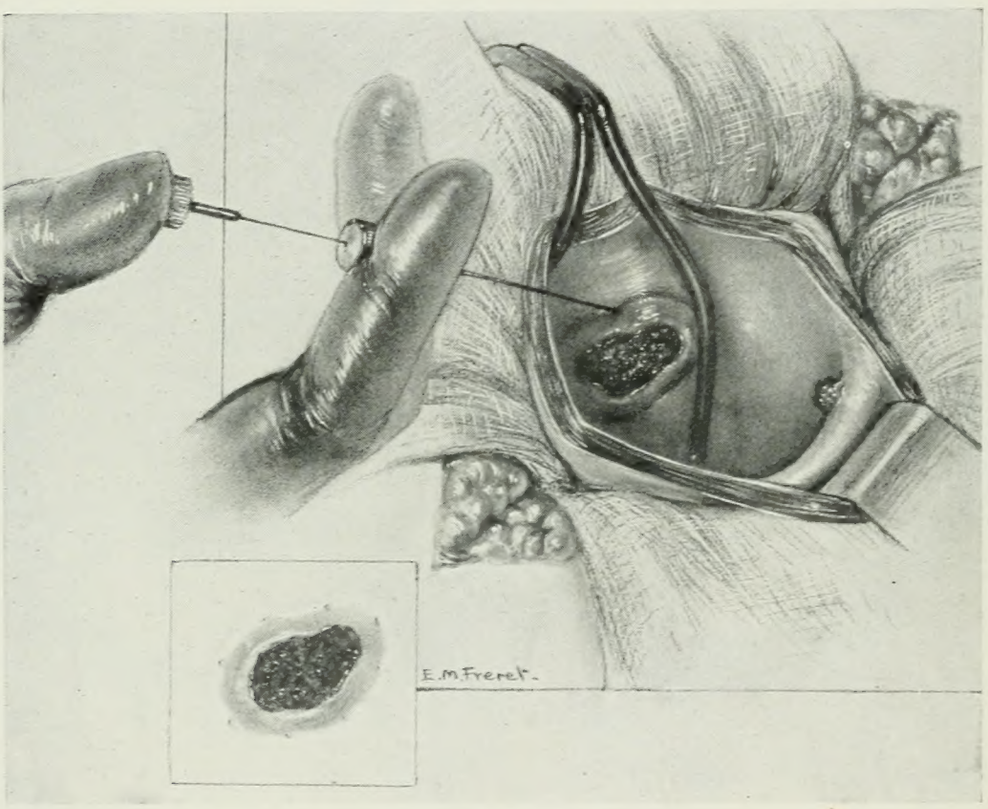

Fig. 4.—Burying radium emanation tubes under direct vision after exposure of carcinoma by suprapubic cystotomy.

Rectal Examination.—If there is extensive induration of the bladder base, that is an indication that the tumor has grown through the bladder. If the tumor or its base is felt, but, between the tumor and the examining finger, is interposed somewhat soft bladder wall the case is still suitable for exploration. In a number of such cases we have removed the tumor from the bladder for various periods of time. The examination should be made with a thin-gloved finger, the bladder must be empty of fluid.

Residual Urine.—This is rarely present if the prostate is not primarily involved and should always suggest the possibility of this.

Kidney Function.—In ten out of fifteen cases (operated upon) the kidney function was reduced. In a few instances this reduction was

*These are not included in this report.

marked, the lowest phenosulphonephthalein output being 5 per cent. in the first hour and 7 per cent. in the second. This reduction in kidney function which occurs in perhaps two out of three cases of carcinoma of the bladder is of importance in determining the length of the operation, the kind of operation and the prognosis. We have had three interesting kidney conditions following the use of radium.

Case I.—J. A. H., who had an infiltrative carcinoma of the right side of the bladder near the right ureter orifice. This was small and operable. It has been destroyed by radium now for four years. He also had retention of urine and a hypertrophied prostate. In the midst of his radium treatment he had a stormy time with retention of urine and pyuria. About a year ago it was determined that his kidney corresponding to the side occupied formerly by the carcinoma was a pyonephrotic sac. Either the carcinoma encroaching upon the ureter or cicatrization by the radium caused this kidney's destruction.

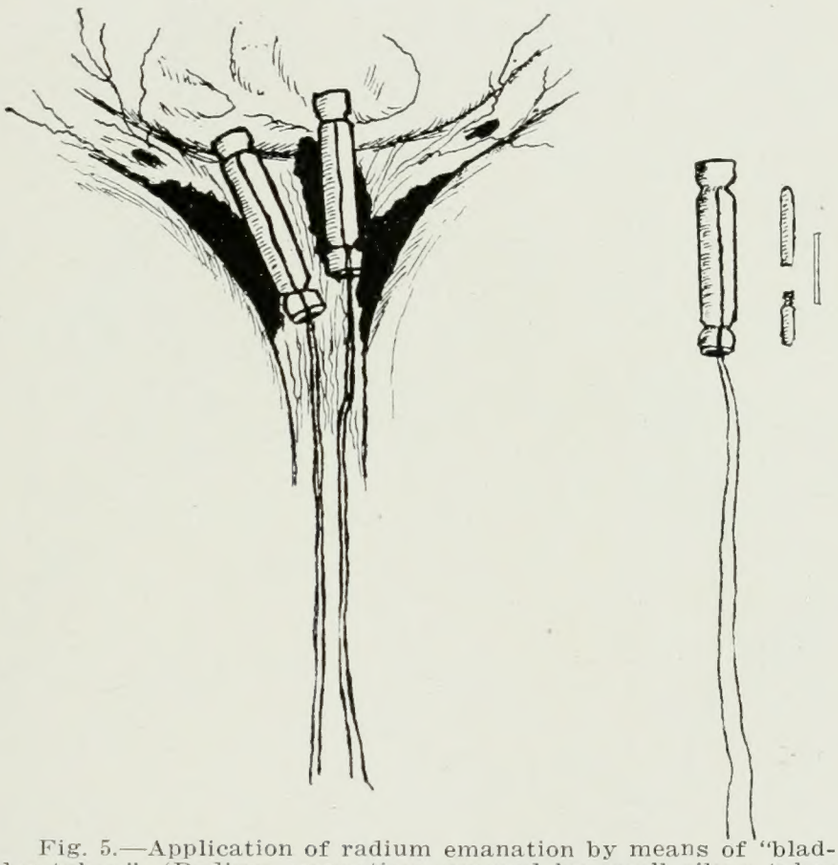

Fig. 5.—Application of radium emanation by means of "bladder tubes." (Radium emanation screened by small silver tubes which are inserted into short pieces of rubber tubing).

Case II.—K. B. Had an extensive carcinoma of her bladder around the right ureter. Previous to radium treatment she had several very severe attacks of renal colic on the side corresponding to the tumor. For ten months subsequent to radium treatment she had no more attacks of renal colic. The tumor was by no means entirely gone, but apparently that portion around the ureter orifice was destroyed, so relieving her of the attacks of colic.

Case III.—B., who had an extensive papilloma of the right side of his bladder. He had previous to operation a phenolsulphonephthalein output of 5 per cent. the first hour, and 7 per cent. the second hour. His bladder was opened suprapublically, the tumor snared off and radium imbedded in the base. For a number of weeks he ran a slight temperature, then considerable temperature and was found to have a large right kidney. His condition became progressively worse. I opened his kidney under novocain and found it to be hydronephrotic with the urine under tension and with pus in the kidney pelvis. This was drained, the patient became better for a number of weeks, then died septic.

Cystogram.—We have used the following technic at the Memorial Hospital to graphically show the tumor and the infiltration of the bladder wall. The patient is placed flat on his back, a catheter is introduced into his bladder, and the contents emptied. With a large syringe the bladder is blown up with air until the patient feels discomfort. The radiograph is immediately taken without withdrawing the catheter from

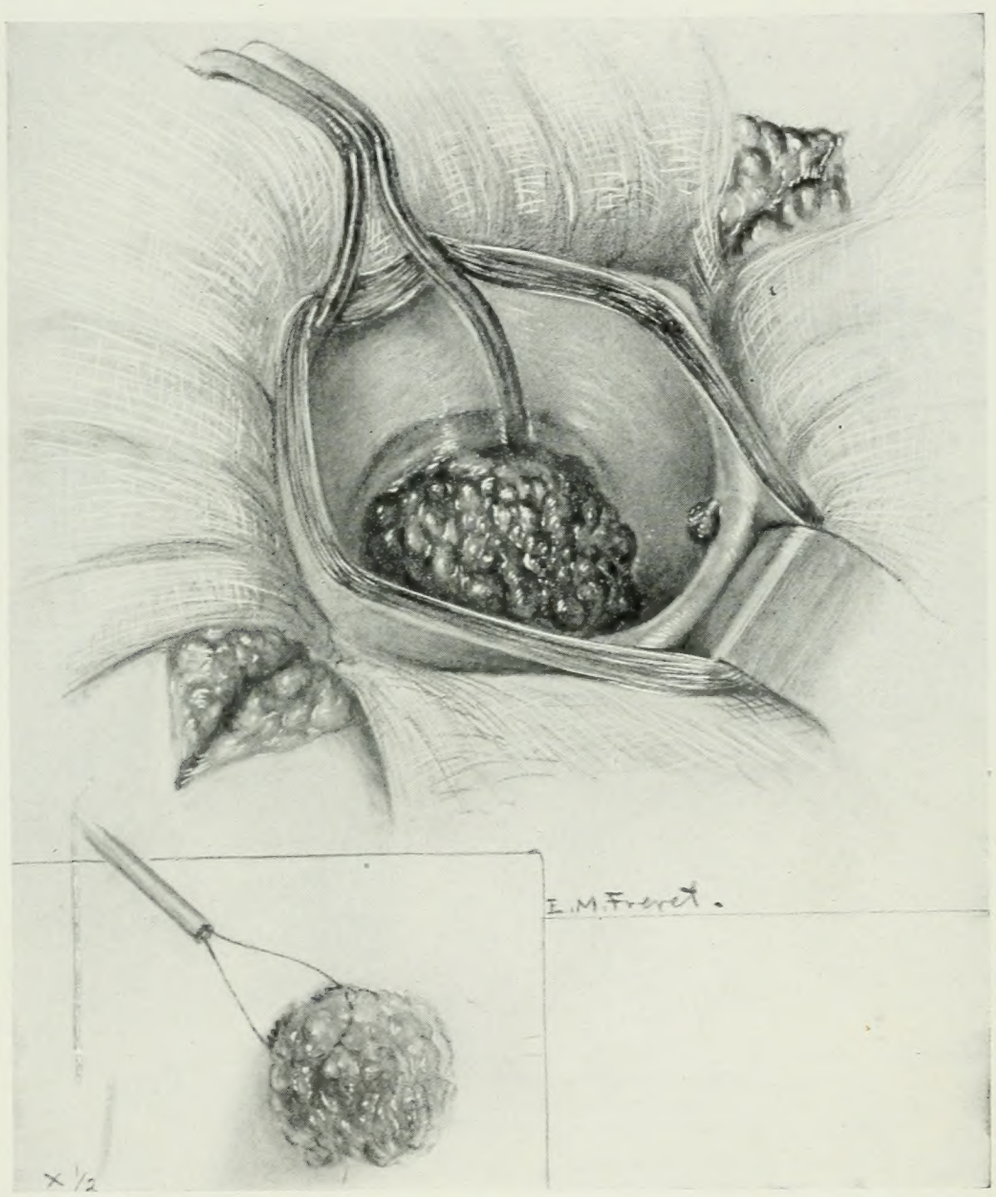

Fig. 6.—Use of special retractor in exposing clearly the carcinoma, especially its base. Snaring off pedunculated growth preparatory to burying radium emanation tubes in its base.

the bladder. We have in many cases compared the findings on opening the bladder with the results shown by cystogram, and find in most cases they pretty accurately correspond. If a tumor is pedunculated its pedicle is not shown by cystogram.

Secondary Urethral Tumors.—We have seen a good many cases of urethral tumors either accompanying or following bladder tumors. I think we often overlook these small urethral tumors having our eye on the major condition. Whether these are real implantations from the bladder or a retrograde lymphatic invasion I hesitate to say. Most of

these urethral implants are of the same structure as the bladder tumor, although I have lately seen a small soft urethral tumor in a patient in whom I had removed an indurated carcinoma from his bladder. I think it safe to consider them as malignant as the bladder tumor.

Fig. 7.—Bladder retractors used in the operative method of burying radium emanation tubes.

INDICATIONS FOR RADIUM.—1. *Local Removal from Bladders*: If the tumor is confined to the bladder it may be suitable for removal by radium. We have removed from the bladder (for various periods of

time) all kinds of carcinomata, *viz.*, infiltrating, indurated, extensive, highly malignant.* This naturally does not mean that we have been uniformly successful; far from it. Different tumors react differently to radium.

2. *Haematuria.*—Radium fairly consistently controls hemorrhage, and may be used for this even if the tumor has gone beyond the bladder.

3. *Retarding the Growth of Tumor.*—The question is often asked, "Even if there is no hope of cure, will not radium retard the tumor growth so a patient may live longer and more comfortably?" Undoubtedly this is true now and again. The cases in which radium does this are so few, however, the failures so many that I believe it unwise to give radium therapy in those cases in which there is no hope of removing the tumor from the bladder.

Reaction of Different Tumors to Radium.—Different papillomata showing precisely the same structure microscopically react differently to radium—some are destroyed easily and some resist. The same is true of papillary carcinoma, although as a rule papillary carcinoma can be destroyed by surface radiation (using large doses of screened radium). Indurated carcinomata are best destroyed by the implanting throughout the indurated area small bare tubes of radium into the base of a tumor and leaving them there. These bare tubes are very caustic, and very local in their action, extending over an area of about one cubic centimetre. In using them even with great accuracy it is possible to miss some carcinomatous area. Therefore we use a combination of the bare tubes (in the depth) and the screened radium (in the surface) in every case of indurated carcinoma.

Determination of Method of Radium Treatment.—I. *Intravesical*: Growths confined to and around bladder neck. Papillomata. Pedunculated papillary carcinoma if pedicle can be reached. Infiltrating sessile growths of no more than 2 cm. in diameter.

II. *Suprapubic*: Growths other than the above and without metastasis. Extensive infiltration of the bladder wall, large and multiple tumors are the indication for section, to which all doubtful cases are submitted.

Intravesical Methods: By means of a flexible spring holder used through the sheath of the Brown Buerger operative cystoscope a hundred or more millicuries of unscreened radium may be held up against the tumor for the period of half an hour while the tumor is being observed through the cystoscope. This may be repeated every two weeks, or less often if the tumor is disappearing satisfactorily. If the tumor looks solid or hard, or has a base which looks indurated, then we may treat it by thrusting into its base or the indurated part, a radium needle screened simply by the steel of the needle. This needle is also on a flexible spring and is used through the operating cystoscope. Needles from 50 to 200 mc. may be used for a period of time up to forty minutes. We must remember that in this method the action is local and caustic. We have in a similar way implanted small bare tubes of radium into the base of a tumor and left them there. For this, bare tubes of 0.5 mc. to

*The largest infiltrating tumor removed was as large as a hen's egg; had grown through the bladder wall and was adherent to the symphysis. This case is described on p. 12.

a square centimetre of tumor are used, and left in place. The action here is still more local and more caustic. We have used all of these methods and combinations of them in various tumors and by all of them have destroyed small or recurrent carcinomata of the bladder. If a tumor is more extensive, if it is papillary in character, if the pathological examination shows pure papilloma, and especially if it be around the bladder neck we often start the treatment by placing into the bladder two tubes of screened radium (.6 mm. silver, 2 mm. rubber). These tubes are inserted through the sheath of a straight cystoscope and tied with a string and left in place for varying periods of hours and then pulled out of the urethra by the attached string. As a rule we use two tubes of 50 mc. for five or six hours. The value of such radiation is first, to see how the tumor reacts to radium; second, to temporarily stop the bleeding to make cystoscopy possible, and third to destroy that portion of the tumor around the internal urethral orifice. If the tumor is carcinomatous and large, and we believe from our examination it is confined to the bladder, then we do the open operation described below.

Suprapubic Application of Radium in Extensive Carcinoma.—Because we were unable to cope with extensive carcinomas of the bladder by the intraurethral method, in June, 1919, we began to open up the bladders in selected cases and implant radium directly into the carcinoma. The technic is as follows:

Gas and oxygen anæsthesia is used. The bladder is prepared previous to operation by washing it out with a 1:4000 acriflavine solution, then draining the fluid out of the bladder and blowing the bladder up with air. The patient is placed in Trendelenburg's position. The skin incision is a long one, extending from the symphysis to the umbilicus. The prevesical fascia is cut transversely at the symphysis and dissected back, the bladder being exposed well down its posterior wall. The urachus is cut, and the exposure extends beyond this. The sides of the wound are screened with gauze soaked in acriflavine (1 to 4000) solution. The bladder is gently palpated so the incision may not go through tumor tissue. Between two clamps the bladder is opened and a three- or four-inch incision is made longitudinally. The cut surface of the bladder is grasped by clamps, the clamps being about one inch apart. The reason for this is that the bladder will otherwise collapse and fall down into the pelvis when retractors are put in it, so making operation impossible. A light is thrown into the bladder and bladder retractors three or four in number are gently placed in the bladder. The retractors which we have used most have been made for us at the Memorial Hospital. They are made of one-eighth-inch steel wire in the form of an open loop. The advantage of these is that the tumor may be seen through the open portion of the retractor, and treated. The tumor being exposed is sponged as little as possible to prevent bleeding and spreading of tumor cells. Alcohol sponges are used. Any protruding portions of the tumor are snared off, using a simple wire snare. If the tumor is flat and not papillary in type, none of it is removed. The reason for snaring off the papillary part is to better expose and treat the base. Indurated parts of the tumor are implanted with radium bare tubes (0.5 mc.) by means of a needle, using two of these to the square centimetre. These bare tubes are not put in the normal mucous membrane, but within a quarter of a centimetre of the edge of the tumor.. Finally, surface radiation is accomplished by means of tubes of radium screened

by 0.6 mm. of silver and two millimetres of rubber placed on the surface of the tumor and held in place either by gauze packing or little hooks on the silver tubes. A string is attached to these tubes, and they are pulled out after an appropriate time. A space 2½ cm. in diameter is radiated by two of these tubes placed longitudinally side by side, 1 cm. apart. To such an area, 500 or 600 millicurie hours is given. Before placing these tubes in, a can of ether is emptied into the bladder to kill any stray tumor cells. The bladder is closed up with plain catgut, the strings of the radium tubes and the packing exiting through the small opening left in the bladder. The gauze screening in the wound is now removed, and ether poured all over the wound. The wound is closed as usual. Two cases operated upon in this manner are here reported to show what can be done in inoperable (aside from total cystectomy) cases.

S. D., male, age thirty-seven. In 1917, nocturnal frequency of urination progressively increasing until he urinated every fifteen minutes. Never haematuria.

November, 1917, a small carcinoma of the bladder was excised. It recurred very rapidly. Shortly after leaving the hospital his frequency was as great as before.

In June, 1919, he came to the Memorial Hospital with complete retention of urine and had to be catheterized. I opened his bladder and found his bladder full of clots and red papillary carcinoma the size of a small orange attached to the left bladder base and lateral wall. The papillary portion of this was cut off with a cautery, and fifteen bare tubes of radium (3 mc. each) were planted in the base of the tumor which was of the size of a silver dollar and which included the opening of the left ureter. A suprapubic tube was left in for a number of days, then removed, the wound healing without trouble. He had burning and frequency for a number of months after operation caused by the radium. Cystoscopy, February 25, 1920, showed a bladder clean of tumor. There was no induration of its bladder base by rectal examination. He had gained thirty-nine pounds in weight and working all the time.

In January, 1921, cystoscopy showed a clean bladder with one or two very small papilloma of his posturethra. These were treated by radium.

H. W., male, age sixty-two. A single haematuria in January, 1920, then clear urine and again, February, haematuria. At this time he was cystoscoped and the diagnosis of "tumor of the bladder" made.

I first saw him in March, 1920. Then he was a well nourished man, had lost no weight, had a nocturnal urinary frequency of two. He passed urine colored with blood. The rectal examination showed slight induration of the middle of the bladder base with a normal prostate. The cystoscopic examination showed a tumor on the right side of his bladder, sloughy on the surface. It was impossible to tell its extent because of the haematuria. He gave a history of having had sugar in his urine but his blood sugar was not increased. He was but a fair operative risk. I opened his bladder and found a tumor on the right anterior wall, solid, of the size of a hen's egg. It had grown through the bladder wall and was adherent to the symphysis. We did not cut into the tumor for a specimen, but scraped off a slight portion of the surface which showed on examination mucus and pus. There was no doubt, however, of the clinical diagnosis of "carcinoma." This was the largest carcinoma that we had attempted to remove. We filled the tumor as accurately as was possible with radium tubes of 0.2 mc., two to a cubic centimetre, leaving these in place. The bladder was drained for a long time because I feared the sloughy results from the radium absorption of the tumor. The patient's recovery was uneventful, barring the fact that he had a persistent suprapubic sinus. Three months after my first operation I cut out the bladder sinus and sewed up the bladder. During this operation I searched with my finger the site of the old tumor, and could find nothing abnormal, barring a slight irregu-

larity about 1 cm. square in the surface of the mucous membrane of the bladder. He was last cystoscoped in February, 1921, and his bladder, while slightly hyperaemic over the site of the tumor from the effects of the radium, showed no tumor. He is in the best of health, and has no symptoms except that he gets up once or twice at night to urinate.

Tables showing the results in both intravesical and suprapubic methods are appended to this article.

Intravesical.—We have removed the carcinoma from the bladder in eleven cases by the intravesical application of radium. The longest case has gone four years and four months with the bladder clean of tumor and proved by cystoscopy.

Suprapubic.—To January, 1921, we have operated upon twenty-nine cases of carcinoma of the bladder. There were no deaths directly after operation, although one died seven weeks post-operation, and one two months post-operation. Some of these patients showed carcinoma so extensive that no radium treatment was attempted. In ten of the twenty-nine cases the carcinoma was removed from the bladder, the longest case having gone twenty months post-operation with a bladder, clean of tumor. Five of the cases have not been cystoscoped post-operation. The remaining fourteen are dead or doing badly and one has not been traced since he left the hospital. There has been but one implantation of tumor in the operative wound in a case which was operated upon before he came to us—so we can divide the responsibility for this.

Examination of the chart will show how very extensive and inoperable all of the tumors were if we exclude cystectomy. I have never seen any operative statistics that at all compare with those of the following table:

EXTENSIVE CARCINOMA OF BLADDER—RADIUM IMPLANTED THROUGH BLADDER OPENED SUPRAPUBICALLY

	No.	Name.	Age.	Date oper.	Description of tumor	Pathology	Previous oper.	Result.
	1	V.	36	June 1919	Papillary tumor, large as orange, base 5x5 cm., of left bladder base.	Papillary infiltrating carcinoma (Ewing)	One	Bladder clean (cystoscopy) 20 months post-op. (Sl. papilloma of urethra.)
	2	K.	54	Jan. 1920	Papillary tumors, indurated base (largest 3x3 cm.) all around bladder neck.	o	o	Bladder clean (cystoscopy) 9 months post-op.
	3	W.	61	Mar. 1920	Solid tumor, ulcerated surface (6x6x6 cm.) on anterior wall of bladder, growing through bladder and adherent to pelvis.	o	o	Bladder clean (cystoscopy) 12 months post-op.
Carcinoma of Bladder...	4	W.	60	Apr. 1920	Pedunculated tumor (small tangerine) covered with incrustations, left bladder wall, indurated base	Papillary carcinoma (Ewing)	o	Bladder clean (cystoscopy) 9 months post-op.
Operated cases	5	G.	50	Apr. 1920	Solid, flat tumor 3x4 cm., within 1 cm. of left ureter	Infiltrating Carcinoma (Ewing)	o	Recurrence after operation treated intravesically. Bladder clean (cystoscopy) February, 1921
Bladder clean on one or more cystoscopies post-operation	6	D.	53	May 1920	Solid tumor, left wall, 2x4 cm. Papillary tumors around bladder neck	Infiltrating carcinoma (Ewing)	o	Recurrence after operation. Treated intravesically (3 times). Mar., 1920 no tumor. Radium slough
	7	T.	59	June 1920	Flat, irregular tumor around urethra (treated by radium before oper.). Small tumor seen at oper.	Infiltrating carcinoma	o	No tumor 6 months post op. Radium slough (cystoscopy)
	8	S	55	July 1920	Papillary tumor, 4x5 cm., of left bladder base. Base indurated	Papillary carcinoma (Ewing)	o	Bladder clean (cystoscopy) 9 months post-op.
	9	W.	50	Aug. 1920	Indurated, ulcerated tumor, 3x3 cm., around sphincter of bladder	Epidermoid carcinoma (Ewing)	o	Bladder clean (cystoscopy) 6 months post-op.
	10	R.	70	Dec. 1920	Indurated, flat, irregular tumor, 3x3 cm., centering in L. trigone & touching bladder neck	Papilloma (Ewing)	o	Bladder clean (suprapubic observation) 2 months post-op.
	1	H.	48	Sept. 1919	Number of hard nodules around bladder base. (Scar of radium in bladder neck from pre-op. treatment)	Papillary carcinoma (Brooklyn Hospital)	One	Eighteen months post-op. has sl. urinary frequency (once at night). No pain. Looks and feels entirely well. Refuses cystoscopy.
Carcinoma of bladder...	2	H.	56	Sept. 1920	Papillary tumor 6x4 cm., posterior to L. ureter. Pedicle infiltrated. Base 3x3 cm.	Papilloma (Ewing)	o	Recurrence post-op. Still treated (March, 1920).
Not cystoscoped since operation	3	B.	49	Oct. 1920	Multiple hard tumors, bladder base & anterior wall; one 2x3x2½ cm.; one 3x1x1 cm.	Carcinoma (Brooklyn Hospital)	One	Not cystoscoped post-op.

EXTENSIVE CARCINOMA OF BLADDER—RADIUM IMPLANTED THROUGH BLADDER OPENED SUPRAPUBICALLY

	No.	Name.	Age	Date oper.	Description of tumor	Pathology.	Previous oper.	Result.
	4	M.	50	Dec. 1920	Indurated ulcerating tumor touching internal urethra 4x3 cm.	Squamous infiltrating carcinoma (Ewing)	o	Not cystoscoped post-op.
	5	R.			Solid, rounded, nonpedunculated tumor, indurated base, touching left side trigone, 7x10 cm.	Papillary carcinoma (Ewing)	o	Not cystoscoped post-op.
	1	R.	59	July 1919	Whole bladder wall carcinomatous, not treated	o	o	Died 5 months later.
	2	H.	42	July 1919	Extensive indurated carcinoma 10x5x2 cm., probably originating in prostate	Epidermoid carcinoma (Ewing)	o	Died 6 months later.
	3	R.	47	July 1919	Indurated carcinoma around bladder neck, probably primary in prostate	Papilloma (Ewing)	o	Died 14 months later of anuria after pyelotomy to relieve obstruction of lower ureter caused by carcinoma.
	4	W.	41	Aug. 1919	Extensive growth of bladder wall, coming from outside bladder(?)	o	o	Died 1 year later.
	5	C.	60	Dec. 1919	Entire vault and sides of bladder infiltrated. Trigone clear	Infiltrating epidermoid carcinoma (Ewing)	o	Died 3 months later.
	6	L.	38	Dec. 1919	Extensive, diffuse papillary tumor of anterior wall	Papillary carcinoma (Ewing)	o	Died at another hospital (three months post-op.) from infarction of prevesical space due to sloughing of bladder wall by radium.
Carcinoma of bladder Operated cases	7	S.	52	Feb. 1920	Indurated carcinoma (3x3 cm.) around internal urethra.	o	o	Died 7 months later.
Patients dead or doing badly or not followed..	8	L.	60	Apr. 1920	Mass size of golf ball, touching internal urethra base, 2x10 cm.	Carcinoma (Ewing)	o	Died 2 months later
	9	D.	69	Apr. 1920	Pedunculated tumor 8x4 cm. (base 3x3 cm.) attached to trigone	Papillary carcinoma (Ewing)	o	Died of uremia 7 weeks post-op. Bilateral pyonephrosis.
	10	B.	43	Apr. 1920	Papillary carcinoma with indurated base (7½x4 cm.) touching right ureter	Papillary carcinoma (Ewing)	o	Operated upon twice. Now six months after 2nd Operation has urinary frequency, but is in fair general condition.

EXTENSIVE CARCINOMA OF BLADDER—RADIUM IMPLANTED THROUGH BLADDER OPENED SUPRAPUBICALLY

	No.	Name	Age.	Date oper.	Description of tumor.	Pathology.	Previous oper.	Result.
	11	R.	19	Apr. 1920	One carcinoma, lateral wall, 5x5 cm. x 1 cm. (thick); 1 carcinoma left trigone & urethra, 7x1 cm.	Infiltrating squamous carcinoma (Ewing)	o	Left hospital in good shape. Cannot be traced since.
	12	O.	50	Apr. 1920	Two sloughy tumors, 2½x1 cm. & ¾x½ cm.	Alveolar carcinoma (Ewing)	Once	Doing badly. Implantation in abdominal wound (Mar., 1921).
	13	B.	60	May 1920	Flat, indurated carcinoma, 10x7 cm.; implant 1x1 cm.	Solid carcinoma (Ewing)	o	Died 3 months post op.
	14	E.	56	Aug. 1920	Sloughy, flat carcinoma, right bladder wall, 3x3 cm.	Carcinoma (Ewing)	o	Five per cent. sugar in urine at time of operation. Died 3 months post-op. of perirectal abscess.
Papilloma bladder	1	W.	55	May 1920	Firm, red, papillary tumor, large as small orange, base 3x3 cm., external to left ureter. A second small tumor.	Papilloma (Ewing)		Bladder clean (cystoscopy)
Operated cases.							o	10 months post-op.
Bladder clean on Cystoscopy	2	Mc.	61	Oct. 1920	Tumor large as tangerine (calcareous incrustations), right lateral wall, base 2x2 cm. No induration base.	Papilloma (Ewing)	o	Five months post-op. no tumor (cystoscopy). Radium slough.
	1	W.	55	Apr. 1920	Bladder filled with papillomata; no induration of bases.	Papilloma (Ewing)	One	Seven months after 1st operation was operated upon 2nd time for suprapubic sinus and more papillomata. Still treated (March, 1921).
Papilloma bladder	2	C.	56	May 1920	Very large papillary tumor 7x7x7 cm., attached to bladder base, posterior to left ureter, base 1x1 cm.	Papilloma (Ewing)	o	Reports well 9 months post-op. Not cystoscoped post-op.
Operated cases not cystoscoped since operation or still treated...	3	P.	63	June 1920	Entire bladder base and lateral walls covered with papillomata; no induration.	Papilloma (Ewing)		Six months post-op. still papillomata. Being treated.
	4	K.	56	Oct. 1920	Pedunculated tumor, 5x4x3 cm. anterior to r. ureter; no induration.	Papilloma (Ewing)	o	Not cystoscoped post-op.
	5	S.	48	Dec. 1920	Entire lower half bladder filled with papillomata; no induration.	Papilloma (Ewing)	o	Not cystoscoped post-op.
	1	B.	56	Sept. 1920	Three papillomata, bladder base, largest 1x1 cm.; no induration.	Papilloma (Ewing)	o	Died 3 months post-op. Pyemia (after pyelotomy for pyonephrosis).

CARCINOMA OF BLADDER TREATED INTRAVESICALLY BY RADIU M. CASES IN WHICH TUMOR HAS BEEN REMOVED FROM BLADDER 1916 TO 1920, INCLUSIVE.

Case.	Age.	Sex.	Evidence of Carcinoma		Extent.	Induration	Urinary frequency D. N.	Wgt. loss	Previous treatment	Radium—Dose—Method.	Result.
			Cystoscopy	Pathology.							
I.C.A.G.	69	F.	Cauliflower, non-pedunculated, sloughy	Carcinoma (Ewing)	Base 3 cm. in diameter over 1. ureter	?	3-4 3-4	0	Fulguration twice	100 mc. 8 hrs. Bladder tube.	Bladder clean 4 yrs. 4 mos. Cystoscopy
E.J.S.	54	F.	Papillary, sloughy in part.	Papilloma (Ewing)	All around bladder neck and trigone.	Vaginal, 5 cm. in diameter.	q. hr. 5-20	?	0	100 mc. 8 hrs. 2 bladder tubes. Repeated twice at 3 mos. interval.	Bladder clean 1 yr. Cystoscopy. Well (letter) 4 yrs.
L.M.	70	F.	Papillary red tumor of bladder base	Carcinoma (Ewing)	Multiple large one on trigone.	Vaginal, s small area	Frequent & pain.	0	Fulgurated 2 years	200 mc. 7 hrs. 2 bladder tubes.	Bladder clean 2 yrs. then recurrence (rapid growth). Removed by radium 1 yr. Radium burn.
J. A. H.	62	M.	Rapidly growing, flat, ulcerated.	Carcinoma (Ewing)	Small, operable near ureter	0	2-3	0	Fulgurated once	180 mc. 6 hrs. 2 bladder tubes. Repeated in 4 mos.	Bladder clean 4 yrs. (cystoscopy). (Kidney no function on side corresponding to tumor).
H.F.R.	68	M.	Sloughy papillary tumor	Papillary Carcinoma (Ewing)	Extensive, bladder neck	?	q. hr. q. hr.	17 lb.	0	100 mc. 8 hrs. 2 bladder tubes. Repeated 6 mos. later for recurrence.	1st, bladder clean 3 mos.; 2nd, bladder clean 1 ½ yrs. Well 2 ½ yrs. (letter).
A.T.V.W.	59	F.	Papillary tumor some slough, left trigone.	Papillary Carcinoma (Ewing)	2x2 cm.	?	2-3 2-3	0	0	100 mc. 6½ hrs. 2 bladder tubes. Repeated 6 mos. later.	Bladder clean once (cystoscopy)
F.H.P.	63	M.	2 tumors, 1 necrotic, 1 red.	0	Around bladder neck.	0	q. 3. hr. 2	0	0	70 mc. 1 hrs. 2 bladder tubes.	Bladder clean 4 mos. (Cystoscopy). Well 2 yrs. (letter).

CARCINOMA OF BLADDER TREATED INTRAVESICALLY BY RADIUM, CASES IN WHICH TUMOR HAS BEEN REMOVED FROM BLADDER 1916 TO 1920, INCLUSIVE.

Case.	Age.	Sex.	Evidence of Carcinoma		Extent.	Induration	Urinary frequency D. N.	Wgt. loss	Previous treatment	Radium Dose Method.	Result.
			Cystoscopy	Pathology.							
G.	61	F.	Tumor, flat, ulcerating, r. lateral wall.	Epidermoid carcinoma (Ewing)	2x3 cm.	o	q. 2 hr. q. 2 hr.	o	o	100 mc. 4 hrs. 2 bladder tubes. Base tubes (2 of 0.5).	No tumor 8 mos. later (cystoscopy). Radium burn.
W.	50	F.	Small, ulcerating, flat, back of l. ureter.	Epidermoid carcinoma (Ewing)	3x3 cm.	o	o	o	o	100 mc. 6 hrs. 2 bladder tubes.	No tumor 8 mos. later (cystoscopy).
H.	50	M.	Red, smooth, rounded tumor near r. sphincter.	Questionable if Carcinoma.	3x3x2 cm.	o	o	o	o	Base tubes (0.5) through cystoscope.	No tumor 1 yr. later (cystoscopy).
S.	53	M.	Multiple, sloughy, around bladder neck.	Carcinoma (?) (Ewing)	Multpile, largest 1x1 ½x3 cm.	o	?	o	o	100 mc. 5 hrs. 2 bladder tubes.	No tumor 2 mos. later (cystoscopy).
					PAPILLOMA OF BLADDER						
C.	60	M.	Bladder filled with grape-like masses, recurring post-op.	Papillary (Mandlebaum)	Bladder vault (?) full.	o	?	o	Operation	2 tubes 50, 8 hrs.	Sl. tumor 3 yrs. 8 mos. later. Treated. No tumor 3 mos. later
Z.	12	F.	Multiple, red tumors around sphincter	Papillary (Ewing)	Multiple one 3x3 cm.	o	o	o	Fulguration	100 mc. 8 hrs. 1 bladder tube.	Recurrence 3 yrs. later. Treated. No tumor 3 mos. later. Died hemorrhage.
R.	63	F.	Multiple, red papilloma trigone.	Papillary (Ewing)	5x5x1 cm.	o	o	o	o	90 mc. 7 hrs. 2 bladder tubes.	Reported no papilloma 1 yr. later (cystoscopy).
O.D.	71	F.	Red, papillary growth behind l. ureter.	o	5x5x5 cm.	o	o	o	o	100 mc. 8 hrs. 2 bladder tubes. Subsequent fulguration.	No tumor 9 mos. later (cystoscopy).

CARCINOMA OF PROSTATE*

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Carcinoma of the prostate presents as many complexities of diagnosis and treatment as any other disease of the urological tract. The internal situation of the prostate, the confusion between carcinoma and adenoma, the quiet, often symptomless, invasion of the prostate by the carcinoma, the urinary retention, the conflict between operative and radium treatment—these are some of the phases. In this paper only the most important problems of diagnosis and treatment are considered. It is especially an attempt to bring up to date the report of radium therapy in carcinoma of prostate as practiced at the Memorial Hospital.

Gross Pathology—Types of Malignancy

The two following histories with their postmortem data represent two types of malignancy between which extremes all variations occur.

Case 1. J. S. W., age 60, admitted to Memorial Hospital September 11, 1919, with a history of frequency of urination and prostatic retention for a number of years.

The examination of his prostate (by rectum) revealed a very large, irregular, stony hard prostate fixed to the pelvis. Indurated masses extended along the right and the left vesicles. The top of these masses could not be felt. The patient was very thin and cachectic. Residual urine 4½ ounces. Radium had no effect that could be determined by palpation upon the carcinoma. Patient gradually grew worse and died December 3, 1919. The postmortem record showed: "Kidneys—ascending suppurative pyelonephritis; prostate—measures 4 by 5 centimeters laterally and 2½ centimeters vertically. Structures are obliterated by opaque tumor tissue which fungates, through base of bladder at trigone, 3 centimeters wide. Rectal wall is slightly adherent but not involved. Peritoneal surface behind bladder base shows superficial subserous nodules. No enlarged lymph nodes were found. The carcinoma has not extended above the seminal vesicles."

Case 2. J. S., age 74, admitted to Memorial Hospital, August 24, 1916. His chief complaint was a tumor mass on left jaw. Seven months previously he had had a severe facial neuralgia, and then a small lump appeared on the left cheek anterior to ear. The lump increased in size. Patient lost weight and strength rapidly, 34 pounds in a "short time." Lately he has had some "stomach trouble." The physical examination showed: no teeth in either jaw; above left molar region of inferior alveolar process is a small area of tumor the size of a 5-cent piece. Extending into adjoining buccal mucous membrane is a hard tumor growth which involves the whole side of the inferior maxilla producing a large tumor of the left cheek. The tumor is hard and fixed to the inferior maxilla. Rectal examination showed the prostate slightly enlarged and very irregular. The left lobe was larger than the right. Small, hard nodules appear on surface, but there is no perivesical enlargement. Diagnosis: *probably primary prostatic carcinoma* with metastases to jaw.

The postmortem showed: kidneys, left pyelitis and chronic productive nephritis; right pyelitis. The bladder showed chronic suppurative cystitis. The left lobe of prostate was slightly enlarged and showed pea-sized nodules projecting from the posterior surface. At entrance to prostatic urethra surrounding orifice were a few soft, pea-sized papillary projections. Running up the spinal column was a series of slightly enlarged lymph nodes becoming more marked in the thorax, and replaced by soft tumor tissue. In the thorax,

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the process from lymph node invaded the body of the fourth and fifth dorsal vertebræ. This process encircles the spine and invades the periosteum of the sixth and seventh ribs largely destroying both. The entire left inferior maxilla is destroyed by a soft tumor process, which invades the periosteum and replaces bone. Diagnosis: carcinoma of prostate; secondary carcinoma of inferior maxilla by invasion through spinal lymph nodes.

In the first case (of low malignancy) notwithstanding the time the disease had been present and the very large prostatic carcinoma, the carcinoma did not go above the seminal vesicles. In the second case (highly malignant), the changes in the prostate were so slight as to make the diagnosis of carcinoma only "probably" yet the metastases were very large and extensive.

Both of these extreme types are rare and all gradations between these are seen. The usual type is a slowly growing tumor which, because of the limiting fascia of Denonvilliers on the one side and the bladder base on the other, generally grows in the line of least resistance, upward into the lymphatics around the seminal vesicles, and metastasizes very early in its life history.

Frequency of Growth Beyond the Prostate in 145 *Cases*

In 2 cases the carcinoma, as far as could be determined by palpation, was confined to the prostate; a third case was borderline. The remaining 142 cases showed extension either toward the vesicles to the bladder, to the lateral walls of the pelvis, or metastases to more distant parts of the body.

Lateral pelvic extension. The commonest extension of a prostatic carcinoma is toward the seminal vesicles. A second, not uncommon extension, may be to the lateral pelvic walls. From either prostatovesicular injunction, a bridge of dense carcinomatous tissue is felt extending to each ramus of the pubes. This is a common extension and one not usually described.

Rectal extension. There were but 3 cases of growth of the carcinomata through the rectal wall at the site of the prostate. This growth was accompanied by vesicorectal or urethrorectal fistulæ and was not to be confused with the perirectal growth often occurring above the seminal vesicles and causing rectal stricture.

Anterior urethral metastases. One of the 145 cases had metastasis in the anterior urethra. This was either a retrograde lymphatic growth or a direct implant into the urethral mucous membrane. In this case metastasis occurred after a Young punch operation on the bladder neck. Carcinomatous tissue broken loose might have formed a transplant. This patient also had a secondary nodule of the head of the penis.

I have seen one other case which had a periurethral metastasis some centimeters back of the head of the penis. In this case there had been no operation on the prostate or urethra.

Distant metastasis. Our records are too imperfect to determine how frequently prostatic carcinoma metastasizes to the pelvis, lumbar spine, lungs, long bones, glands, etc. Bumpus* has lately published records on the frequency of these metastases.

*Carcinoma of the prostate. Surg., Gynec & Obst., 1921, xxxii, 31.

Prostatic Carcinoma Secondary to Bladder Carcinoma

A bladder carcinoma usually starts in the mucous membrane of the bladder, and grows in the line of least resistance, that is, into the cavity of the bladder. Nothing hinders its growth in this direction. So having ample space within which to grow, it metastasizes late. When the bladder contracts to expel urine, the mucous membrane folds up and there is not much pressure exerted upon the tumor. A prostatic carcinoma on the other hand has no space in which to grow. In addition to this it is limited posteriorly by the dense fascia of Denonvillier and anteriorly by the less dense fascia of the bladder base. This tension, so to speak, in which the prostatic carcinoma is held, is one factor in causing it to extend beyond the prostate and metastasize early, and it metastasizes or extends most often upward between these two limiting fasciæ. Probably a contributing factor to early metastasis is the pressure exerted upon the carcinoma when the bladder sphincter contracts at the end of each act of urination. Because of these conditions it is rare for a bladder carcinoma to grow by the difficult route and invade the prostate, but rather common for a prostatic carcinoma to break through the fascia at the bladder base and invade the bladder. The following case is the only one of the series in which the picture was that of prostatic carcinoma but the pathological report showed a squamous-celled carcinoma undoubtedly originating in the bladder.

G. G. H., age 60, first seen July 5, 1920. In October, 1919, he suffered with frequency of urination. February, 1920, he became impotent. He never had hæmaturia.

The prostate shows a hard tumor mass of the posterior lobe of the prostate 2½ by 3 centimeters, stony hard, fixed, and irregular and one cannot feel above the prostate to determine the condition of the vesicles. He has complete retention of urine.

In December. 1920, a suprapubic prostatomy was done to relieve retention of urine. All around the internal urethal orifice were irregular carcinomatous nodes, very extensive, forming valleys and hills. The whole bladder base was indurated, a typical picture of a prostatic carcinoma growing into and behind the bladder wall. The patient died uræmic, in January, 1920. The pathological report (Dr. Ewing) follows:

"The tumor has the structure of an epidermoid carcinoma, the cells being broad, flat, and mostly of distinctly squamous character. It shows none of the glandular features of prostatic carcinoma, and it appears quite improbable that it has any other origin than from the bladder mucosa.

"The radium changes are notable. The first chromatism, often followed by disintegration of the nuclei. Many of these cells form giant masses. Hydropic swelling is also present. Later the cell groups break up, and become very hydropic, while the surrounding connective tissue reacts with production of much cellular granulation tissue. Finally the tumor cells disappear, often leaving giant cells or points of necrosis, much resembling miliary tubercles."

Early Symptoms

1. *Disturbance of urination.* Of 145 cases, 115 had as a first symptom either dribbling, dysuria, nocturia, frequency, difficult urination, or retention, or a combination of these; 11 had, as a second or subsequent symptom some disturbance of urination.

2. *Haematuria.* Eight had hæmaturia as a first symptom, and 25 as a second or subsequent symptom. Of 33 cases which had hæmaturia as a symptom it is definitely stated that the bladder had a secondary carcinoma in 18.

3. *Pain* (not associated with urination). Seven had pain as a

first symptom—3 in the back, 1 back and hip, 1 pain in heel, 1 in prostate, 1 abdomen; 5 had pain as a second symptom. One had pain in groin, 1 pain in buttocks, 1 sciatica, 1 in thigh, 1 in leg.

One patient had as a first symptom œdema of legs; 1, a swollen testicle; 1, constipation; 1, bleeding from rectum.

There is nothing in the symptoms that can distinguish carcinoma from nonmalignant enlargement of the prostate, although in the latter a history of hæmaturia is somewhat more frequent.

Age—129 Cases

30 to 40 years	2
40 to 50 years	5
50 to 60 years	33
60 to 70 years	59
70 to 80 years	27
80 to 90 years	3

Here again the age incidence runs nearly parallel to that of hypertrophy of the prostate.

Time Elapsed Between Time First Seen and the First Appearance of Symptoms

In 93 cases of prostatic carcinoma with the growth extending beyond the prostate, the time elapsing between time first seen and the first appearance of symptoms is—

1 to 2 months	15
2 to 4 months	12
4 to 6 months	11
6 to 12 months	19
12 to 18 months	7
18 to 24 months	8
24 to 36 months	7
36 to 48 months	4
48 to 60 months	6
60 to 72 months	3
72 plus months	1

One unusual case was that of a patient with extensive carcinoma of the prostate who had a prostatectomy for prostatic carcinoma 9 years before.

The hopelessness of curing many cases of carcinoma of the prostate if we do not radically change our method of approach is shown by these figures. Notwithstanding that 1 out of 7 cases came within the first 2 months after the appearance of symptoms, that 1 out of 3 cases came to us within 6 months, and 2 out of 3 within the first year of symptoms, in all of these cases the carcinoma had grown beyond the prostate. *We are inevitably forced into the conclusion that regular examination of the prostate of all beyond the age of* 50, *irrespective of the appearance of symptoms, is the only rational method whereby we may hope to get these cases early.*

Examination. The routine examination includes rectal palpation of the prostate with a thin-gloved finger, with and without a sound in the urethra. Special attention is paid to perivesical induration, or

lateral bands to the pelvic walls. Stricture of the rectum occurs high above the vesicles as pointed out by Geraghty, and normally can just be reached with the tip of the finger. The superficial lymph nodes are palpated as is also the penis, for carcinoma. Any swelling of the legs is noted.

The amount of residual urine is measured as also the kidney function. Cystoscopy is done. It is not practicable to radiograph the whole body for metastases to the bones. As metastasis most often attacks the lumbar spine and pelvis, one roentgenogram is taken showing both of these. This roentgenogram may also be used to exclude stone of the prostate, the one condition which most simulates carcinoma. I have on one occasion used a long needle inserted through the perineum into the prostate (novocaine anæsthesia) to make the differential diagnosis between stone and carcinoma. We found that the needle very distinctly grated upon the prostatic stone. Of the 145 cases of prostatic carcinoma seen at the Memorial Hospital, I have never come across a stone in

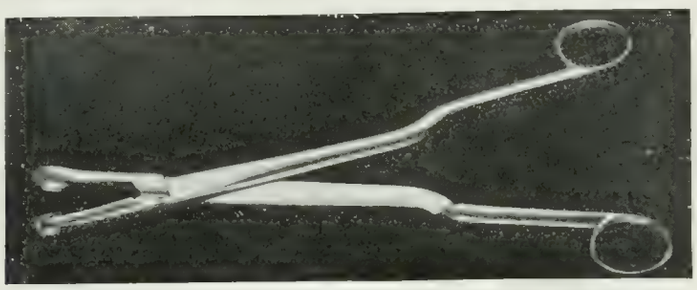

Fig. 1.—Punch used for suprapubic removal of carcinomatous prostatic base.

the prostate. And in all of these the prostatic region had been either radiographed or needled.

Pathological Examination

We have developed at the hospital* a needle which has proved to be of value in the diagnosis of doubtful cases. This needle has a small cutting screw at the point with which prostatic tissue is obtained. The needle is inserted through the perineum (novocaine anæsthesia) into the prostate, a finger in the rectum guiding it. We have used this needle 33 times, in 16 of which prostatic tissue was obtained, 9 of these proving to be carcinoma. It should only be used in cases in which the diagnosis is in doubt.

Technique of Radium Application.

1. *Prostate needle.* The technique first used at the Memorial Hospital in October, 1915, is still with us the most efficient and least painful method of destroying carcinoma of the prostate. A steel needle 10 to 15 centimeters long of No. 18 gauge is used, 50 to 100 millicuries of radium are placed in the end (terminal 3 centimeters) of the needle. Under novocaine anæsthesia with a guiding finger in the rectum the needle is inserted through the perineum into one of the lobes of the prostate. Then at the end of the treatment for that lobe the needle is withdrawn from the prostate (but not entirely out of the perineum) and inserted into the second lobe. A carcinomatous mass 2 centimeters in diameter will stand an initial radium dose of 300 to 400 millicurie hours.

*Dr. Goeller of our staff is responsible for this.

This may be repeated in smaller dose in 2 to 3 months. We have in certain cases used smaller doses at shorter intervals (25 to 50 millicuries every week). But I have no evidence that this method does any more than the above.

2. *Seminal vesicles—needles.* The seminal vesicles are radiated routinely if the size of the prostate does not prevent their being reached. Sometimes they are more easily reached through the rectum than by the perineal route, and in some cases we have so radiated the vesicles. A guiding finger is put into the rectum, and a small cannula is inserted up to the vesicles. The needle is put through the cannula, and so into the vesicle. The lower rectum is previously cleansed with soap and water. We have had no infections of the vesicles following this rectal method.

3. *Bare tubes in prostate and seminal vesicles.* Bare tubes of radium (small doses of radium unscreened except for glass container, and therefore localized and caustic in action) have been used both in

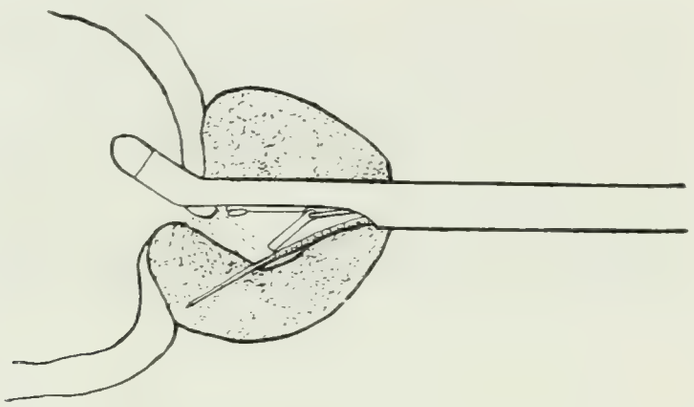

Fig. 2.—Method of inserting bare tubes of radium into carcinomatous prostatic base to relieve residual urine.

the prostate and in any extension beyond the prostate, but have proved not as efficient as the "needle method," and are more painful.

4. *Urethral.* The use of radium in the prostatic urethra has been limited to cases in which carcinoma has directly invaded the urethra. Tubes of screened radium (rubber, 1 millimeter; silver, 0.6 millimeters) 2 centimeters long are attached to a linen thread and inserted into the bladder through the sheath of a urethroscope. The urethroscope is removed and the tubes pulled out into the prostatic urethra by the attached thread. When the treatment is finished the tubes are pulled out of the urethra. Two hundred millicurie hours is a maximum dose. This may be varied by using the silver tube of radium in the end of a urethral catheter.

5. *Rectal.* We have treated but a few cases with screened radium in the rectum. This method does not seem to be as efficient as the "needle method" and produces more pain.

6. *Residual urine.* In most cases the residual urine can be prevented from increasing and in a few it can be decreased by the "needle method" of radium treatment.

If this has no effect and the presence of residual urine causes alarming or intolerable symptoms then we resort to—

a. Bare tubes of radium in the bladder neck. A bare tube of

radium (6 millicuries) is placed in the end of a flexible needle. This needle by means of a McCarthy urethroscope or Buerger operating cystoscope may be plunged into the prostate at the lower part of the bladder neck. By a plunger the bare tube is pushed out of the needle into the prostate and left there. Its action is local and caustic.

b. If the residual urine does not reduce after this then we resort to the Young punch operation or suprapubic drainage or suprapubic partial prostatectomy.

7. *Pain.* Pain caused by growth of the carcinoma around pelvic or spinal nerve has rarely reacted to radium or x-ray treatment.

8. *Swelling of legs.* This symptom caused by pressure of the carcinoma on the common iliac vein has been successfully combated by the radium pack. This is placed on the abdomen and centered over the vein compressed; from 10,000 to 15,000 millicurie hours are given.

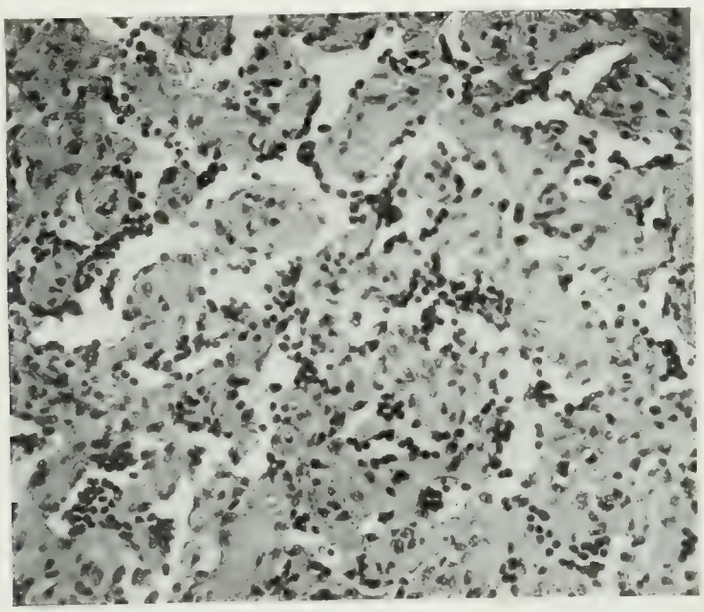

Fig. 3.—Radium changes in epidermoid carcinoma of bladder. Carcinomatous cell groups breaking up.

9. *Rectal stricture.* I have had one case in which I inserted bare tubes (2 to 5 millicuries) into one segment of the stricture. They are inserted through the rectum. This procedure relieved the constipation and made unnecessary a colostomy operation.

Results of Radium Treatment

Report of 5 cases of 145 which have gone 3 to 5 years after first radium treatment, and have shown regression of the carcinoma—

Case 1. C. D., age 59, first seen October 15, 1915. Complained of loss of strength and flesh (some 25 pounds) and night frequency (from 3 to 4 times) for 4 months. He has had pain in right thigh for 5 years. Prostatic examination (with Dr. Keyes) revealed a large, hard, fixed, irregular prostate, each lobe as large as an English walnut. The left lobe was more prominent than the right, and there was but little extension toward the seminal vesicles as far as could be felt. No residual urine. A radium needle of 50 millicuries was placed in each lobe of his prostate for 6 hours, on October 20, 1915.

January 14, 1916, the patient has gained about 10 pounds. Examination of the prostate reveals marked shrinking of the carcinoma. Sixty millicuries of radium (by needle) was placed for 4 hours in each lobe of the prostate.

February 18, did not get up at night to urinate, and had gained 8 pounds.

Slight induration at the base of the prostate. Right lateral lobe treated for 86 hours with a needle of 30 millicuries of radium.

February 27, 1919, up twice at night, working a full day. Weight the same; 64 millicuries of radium in left lobe 6 hours.

November, 1919, up at night, none. Weighs 127 to 130 pounds. Prostate and vesicles feel entirely normal (examination with Dr. Keyes).

January, 1921, 5 years and 3 months after first radium and 2 years and 3 months after last radium, prostate and vesicles normal. Patient in excellent condition.

Case 2. A. S., age 66, first seen October 10, 1916. He had night frequency of urination for 2 years. He now dribbles by night, and urinates every 2 hours by day. Prostate very large, and somewhat irregular but not suggestive of carcinoma. Residual urine, 1,000 cubic centimeters. Cystoscopic examination shows a horse collar prostate. Dr. Keyes did a prostatectomy and Dr. Ewing reported that the specimen showed carcinoma.

November, 1916, the patient had 50 millicuries of radium for 8 hours in what remained of the prostate.

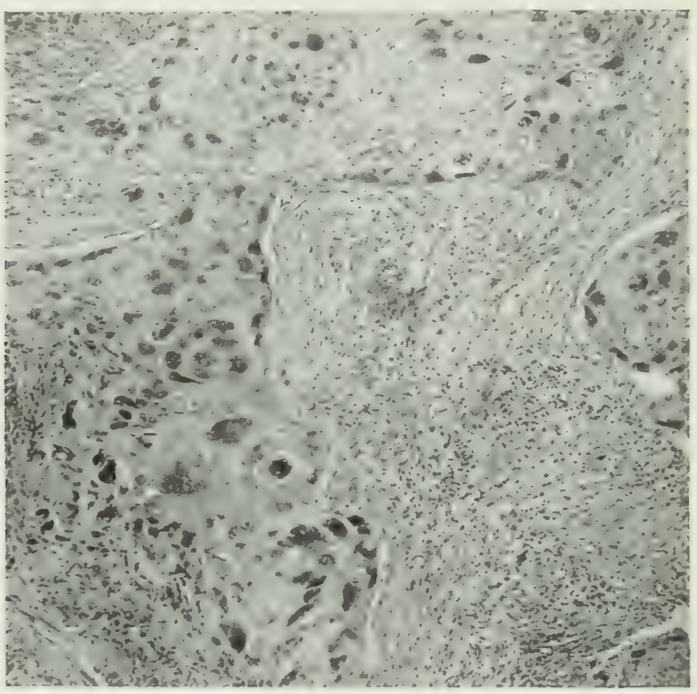

Fig. 4.—Epidermoid carcinoma of bladder growing into prostate and clinically giving picture of prostatic carcinoma.

January, 1917, increased frequency for the past three or four days. At night urinates every half hour. Prostate feels slightly lumpy in lateral lobe. He had another treatment of radium at this time.

February 3, patient had retention of urine, and had to be catheterized three times a day. Radium treatment.

February 27, patient had complete retention of urine, and a permanent suprapubic tube was put into his bladder.

June 20, the patient has had severe pain in his prostate in the last 2 months requiring morphine. The examination shows a prostate irregular, scarred and carcinomatous. The vesicles are indurated and especially the left.

October 15, the patient is in excellent shape physically. He has a collection of calculi around his suprapubic tube. The prostate is flat, the left seminal vesicle has some lumps in it, and is slightly indurated.

January, 1918, radium in left seminal vesicle and prostate.

April, 1918, the patient is in such good shape that I sewed up his suprapubic opening and he left the hospital emptying his bladder.

June, 1919, in the best of shape (examination with Dr. Keyes). There is the same ridge in the left vesicle, the patient empties his bladder, and his prostate feels normal. He is not treated with radium because it is a qustion if he has any carcinoma left.

January, 1921, 4 years 3 months after first radium and 3 years after last radium, examination the same as in June, 1919. Patient in excellent condition

Case 3. M. B. P., age 64. In January, 1916, a prostatectomy was done by Dr. Downes at St. Luke's Hospital. The prostate was found on pathological examination to be carcinomatous. His urethra did not stay open after the prostatectomy, the patient beginning to have increasing retention of urine, and his bladder neck was fulgurated in the attempt to keep the prostatic urethra open. He was first seen by me on April 2, 1917. At that time he had a certain amount of residual urine, but I was unable to get a Phillips' whip into his bladder. Prostate was large and soft. Could not feel above it. There was obstruction in the prostatic urethra. The suprapubic wound drains irregularly. He was treated with 50 millicuries of radium in the right lobe for 6 hours, and was similarly treated in the left lobe.

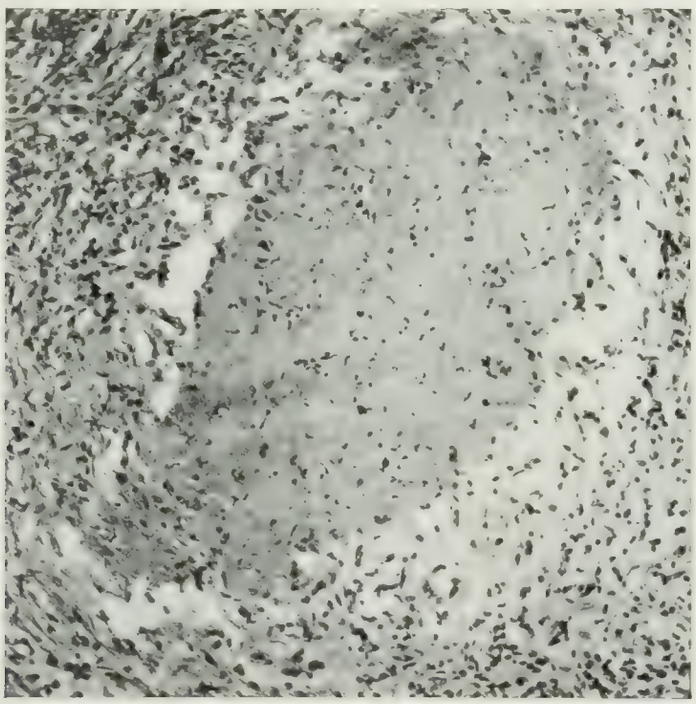

Fig. 5.—Radium effect in epidermoid carcinoma of bladder showing necrosis.

May 4, urinates twice at night, and can go 5 hours without urinating. Before the radium he urinated every 1 to 2 hours.

June 5, 60 millicuries of radium in the right and left lobes of the prostate, each 6 hours.

October 27, up once at night, and more radium to the right and left lobes of the prostate.

March 1, 1918, 3 weeks ago, 50 millicuries of radium for 7 hours and 15 millicuries of bare tubes imbedded in the right side of the prostate. This burned him constantly, and was probably too large a dose.

August 16, 1919, has a residual of 3 ounces. I get a No. 22 French into his posterior urethra. Suprapubic wound still open at times. Urine is very foul.

December 5, 19119, goes 5 hours without urinating at night. Very small hard lump in left apex of the prostate. Is it carcinoma? He has had no radium for 1 year and 9 months; the rest of the prostate and vesicles show nothing. He is the picture of health (examination with Dr. Keyes and Dr. Mohan.)

April, 1921, 4 years after first radium and 3 years and 2 months after last radium condition continues excellent. His suprapubic wound leaks at irregular intervals. Residual ½ to 2 ounces.

Case 4. P. J. H., age 55, first seen July, 1917. Urinary frequency has been present for 3 weeks; by day every hour, by night 6 to 7 times. There is some pain in left groin and testicle and at end of urination. He has lost 10 pounds in weight. Rectal examination shows a not very large prostate, but very hard and irregular carcinoma running into left vesicle (confirmed by Dr. Keyes). Cystoscopy shows an irregular bladder base and irregular bulging of prostate into bladder. Residual none. A steel needle holding 95 millicuries of radium was placed in left prostate for 4 hours. Lost track of until May 7, 1920. (He had during this interval been operated upon for osteomyelitis of skull.) Prostate feels absolutely normal. Both vesicles sclerosed (confirmed by Dr. Keyes). Urinates once at night and five times by day. In excellent health.

May, 1920, bare tubes of radium were placed in the vesicles.

January, 1921, 3 years 5 months after first radium and 1 year after last radium condition remains excellent and same.

Case 5. Borderline case. J. C., age 70, first seen in February, 1916. He gave a history of urinary frequency, chiefly at night (3 or 4 times) for the past 6 months, then acute retention. Patient has lost about 8 pounds. Rectal examination showed a flat irregular prostate with prominent nodules at prostatovesicular junction extending into the vesicles. He was treated several times with radium needles through the perineum. He had no more attacks of retention, his general health improved, and his prostate remained soft and irregular but showed nothing to justify treatment.

In December, 1919, the left vesicle seemed slightly enlarged, and radium was recommended as it was feared the growth might be carcinoma. The prostate was flat and soft.

In August, 1920, patient had an attack of severe pain in the back and left side and was confined to bed. I saw him then when he looked near death, was confined to bed with what was thought to be involvement of his spinal cord by the carcinoma. His prostate felt as normal as in December, 1919.

Reported up and well in January, 1922.

In these 5 inoperable cases the prostates and vesicles are somewhat irregular, scarred, but otherwise normal. They are the only cases which have gone a sufficient length of time since their first and last treatments to report. They all show marked regression of the disease.

Results in Two Cases in Which the Carcinoma Was Confined to the Prostate Out of 145 *Cases Seen.*

Case 1. J. A. H., age 61, first seen in August, 1919, with a history of dysuria for 15 months, a small urinary stream, and frequency of urination, and then finally complete retention. He came to the Memorial Hospital from Bellevue Hospital with a retention catheter in his bladder. His prostate was hard, regular, the size of an English walnut. No induration around the seminal vesicles.

On September 5, by means of the cystoscope, a bare tube of radium of 6 millicuries was placed in the median lobe of his prostate.

On September 23, the residual had fallen to 1 ounce, and he got up 2 to 4 times at night to urinate, and at times during the day goes 4 hours without having to urinate. Because of some lumps in his prostate more radium in the form of bare tubes was applied on September 30. Following this treatment he began urinating every half hour by day and night notwithstanding the fact that his residual urine was only half an ounce. He became steadily worse and finally died uræmic. He had chills and fever for a couple of weeks before his death, and his death was probably due to infection from his prostate and to uræmia.

Case 2. (borderline case). J. W. C., age 71, first seen December, 1919, with a history of hæmaturia 9 months previous. Following this he had frequency of urination and urgency. When seen his night urination was 6 to

7 times. Urine has been steadily bloody, for the past 40 days. Residual urine 2 ounces. His prostate was as large as a hen's egg, a hard single lump. No enlargement around the seminal vesicles. He has had 2 treatments of radium needles in prostate. The growth has very markedly gone down. Patient is still under treatment.

One patient died uræmic and the second is still under treatment.

Result in Very Extensive Carcinoma of the Prostate With Complete Regression of the Carcinoma (Postmortem Report)

G. T., age 50, first seen at the Memorial Hospital, August 23, 1919. Three weeks ago, partial resection of the bladder for carcinoma was done at another hospital. The carcinoma of the bladder was presumably secondary to a carcinoma of the prostate. When the patient was first seen the prostate was very hard, the size of a tangerine, with a number of very hard nodules in it. The vesicles and the base of the bladder were involved by growth. He came to the hospital with a suprapubic drain. Cystoscopy showed a recurrence at the site of the bladder resection. He was treated with radium and lost track of up to January, 1920.

When seen in January, he had a recurrence in the abdominal incision—3 large lumps, each the size of an English walnut, which were treated with bare tubes of radium.

In January, he was almost exsanguinated because of hæmaturia, and his bladder was again treated with radium.

February, 1920, he had a carcinomatous mass from the symphysis to the anterior superior spine on the right side. On the left side was a mass in the inguinal region 8 centimeters wide from the symphysis midway to Poupart's ligament, an enormous carcinoma of the lower abdomen. This was treated with radium.

In May, 1920, all the abdominal masses had entirely gone and his prostate was markedly shrunken.

In November he went on an auto trip, became chilled, and could not void. An outside doctor tried to pass catheter; 10 days later the patient died.

Postmortem examination showed the following (Dr. Ewing):

"A section from various portions of the bladder, prostate, pelvis, and lumbar lumpy nodes failed to show any trace of carcinoma. The walls of the main bladder cavities were everywhere lined with a slough which was very extensive, a diffuse phlegmonous inflammation. The lungs showed purulent bronchitis and pneumonia; the kidney, acute nephritis; prostate, necrosis.

Results in Suprapubic Prostatotomy to Relieve Retention.

This operation has been done in the following way:

Through a suprapubic opening the lower part of the bladder neck has been bitten out with a long rongeur forceps. The operation, aside from using the forceps to bite out the carcinoma, is done precisely in the same way that a suprapubic prostatectomy for adenoma is performed. I have done it only in cases of urinary retention (generally complete) which could not be managed by catheter or which could not be overcome by any of the other described methods. In all cases in which it was done the carcinoma was very advanced. Eight cases in all have been operated upon. Seven cases left the hospital after operation, 1 died in the hospital 2 months postoperative from the growth of the carcinoma around the ureters and failing kidneys. Three were lost track of, after they left the hospital. Two patients went 2 years and 3 months emptying their bladders, and then died. One of these had partial daily incontinence of urine. Wherever practicable the prostate had been thoroughly radiated for a number of months previous to the operation.

Results in Cases Treated by Radium Needle in Prostate in Which Residual Urine Has Not Varied Over a Number of Years

Case 1. No residual, October, 1915. Treated by needle in prostate, never any residual to January, 1921.

Case 2. No residual, but 1 attack of acute retention, February, 1916. Radium needles in prostate, never any residual and no attacks of retention up to August, 1920.

Case 3. Operation removed carcinoma from bladder neck secondary to prostatic carcinoma, May, 1916. Radium needles in prostate. Up to April, 1919, no residual urine.

Case 4. Operative removal of carcinoma of prostate, October, 1916. Several acute retentions followed this. Then retention catheter, Radium needles in prostate. From April, 1918, to January, 1921, no residual urine.

Case 5. Residual 6 to 8 ounces, October, 1917. Radium needles in prostate. April, 1918, residual 1½ ounces. January, 1921, residual again 8 to 10 ounces.

Case 6. Residual, April, 1917, could not be determined as no instrument could be introduced into bladder. Radium needles in prostate. August, 1918, to January, 1921, residual 1 to 3 ounces. A No. 22 French catheter may be introduced into bladder.

Case 7. No residual, July, 1917. Radium needle in prostate. No residual, January, 1921.

These are 7 cases out of the first 43 (cases in 1916 and 1917) which are still living, and which have been observed long enough to give an accurate idea as to the effect of radium on maintaining the capacity of the bladder to empty itself. In none of them has the residual urine increased and in 1 (Case 6) it probably has decreased.

Results of Radium (Bare Tubes) in Bladder Neck to Reduce Residual Urine

Case 1. P. D. April, 1918, residual urine 260 cubic centimeters. He had 7 millicuries (bare tubes) of radium, applied in the lower part of bladder neck. In July, 1918, he had no residual urine.

Case 2. J. A. September 1, complete retention for a number of weeks. Retention catheter September 5. A bare tube of radium 5 millicuries in bladder neck. September 23, residual urine, 1 ounce. October 21, residual urine ½ ounce.

Case 3. J. C. Complete retention for 2 weeks. Retention catheter. Bare tubes of radium 6½ millicuries in bladder neck. Five days later he emptied his bladder and continued to do so for 6 months.

We have tried this method in 4 other cases with no effect on the residual urine. It is a procedure not without danger, as patient who had an extensive carcinoma of the prostate with foul urine and complete retention died 2 weeks after bare tubes were placed in the bladder neck. He died outside of the hospital.

Before the tubes are applied the patient's bladder should be gotten as clean as possible, and the kidney function determined. He should be in the hospital.

Young Punch Operation

This has been performed in 4 cases; in 2 without success; in 1 the patient went from a complete retention of urine to 1 to 2 ounces of residual urine, but died 2 weeks after the operation from infection of his kidney. The fourth patient left the hospital emptying his bladder within an ounce. One year later he was heard from, and at that time

the suprapubic fistula had reopened so the success of the operation could not be determined.

Summary of Methods to Reduce Residual Urine in Carcinoma of the Bladder

Sometimes the needle method in the prostate reduces the residual urine; sometimes the bare tube in the bladder neck does this, but this method is accompanied by considerable pain and some danger. Occasionally the Young punch operation works, as does nearly always the major operation — the suprapubic cutting out of the lower part of the bladder neck. The problem is the most difficult one we have to deal with, and the ideal procedure in intractible cases has not yet been found.

Results in Reduction of Swelling of the Legs Caused by Metastatic Carcinoma

We have had 2 cases in which, by means of a radium pack, the swelling of one or both legs has been reduced. In 1 of these patients who had swelling in one leg, and considerable disability, the swelling reduced 1 month after the radium pack, and the patient lived in comparative comfort until he died of a cerebral thrombosis. In another patient who had swelling of both legs and œdema as far as the umbilicus, the application of 1 radium pack over the right lower abdomen succeeded in reducing the œdema within 1 week after its application. Both of these cases had very extensive carcinoma of the prostate and no attempt was made to treat the carcinoma itself.

Conclusions

1. In but 2 per cent of cases of carcinoma of the prostate seen at the Memorial Hospital is the carcinoma apparently confined to the prostate.

2. Routine prostatic examination of all patients beyond the age of 50, irrespective of symptoms, is the only rational method whereby we may hope to make a diagnosis of prostatic carcinoma early in the disease. In all doubtful cases a speciman of the prostate for pathological examination should be obtained with the speciman needle.

3. The results of radium treatment of carcinoma of the prostate are superior to operative removal both in causing regression of the disease and in coping with urinary retention.

THE TREATMENT OF CARCINOMA OF THE PROSTATE*

By JOHN H. CUNNINGHAM, M.D., Boston.

The object of this communication is to touch briefly upon the clinical course of carcinoma originating in the prostate; to refer to certain features in connection with the diagnosis and what may be done to relieve the condition.

The disease is probably more common than supposed, and the statistics of recent years show that somewhat more than 20 per cent. of prostatic obstructions are due to this cause.

In 1908 Dr. F. S. Watson and myself (Watson & Cunningham) published the operative results by all methods in carcinoma of the prostate up to that time, and there was but one patient who had lived more than four years. The average length of life in the Mayo series recently recorded by Bumpus (*Surg., Gyn. and Obstet.*, Jan., 1921) was 3½ years from the date of the first symptoms. Certainly not a brilliant record!

Since radium therapy has been added to the treatment of carcinoma in general it has, in the hands of a few, been extensively employed in connection with the treatment of carcinoma of the prostate, which has improved the situation somewhat.

Carcinoma of the prostate possesses the same general problem as carcinoma elsewhere, together with certain special features dependent upon its location; producing symptoms of prostatic obstruction.

Considering the subject purely from the clinical aspect, there are two important features, differing entirely from one another, which have a most important bearing upon the symptomatology and course of the disease. The one, metastases, is in most respects the same with carcinoma of the prostate as with carcinoma elsewhere, differing only in certain features because of their location deep in the pelvis and abdomen where they may develop and not be evident until well advanced. The other feature is the development of the growth in the prostate, producing prostatic obstruction with a resulting residual urine and back pressure in the kidneys, with or without urinary infection; or in other words, the same sequence of events as occurs with benign prostatic obstruction.

The most unfortunate feature in connection with carcinoma of the prostate is the fact that the primary focus in the gland may develop so slowly as not to cause symptoms of prostatic obstruction before widespread metastases occur. In fact, the majority of patients seeking medical aid for the symptoms of prostatism due to carcinoma of the prostate generally show well-established metastases at that time, which make the surgical problem, in most instances, a purely palliative measure.

There is also a group of patients with carcinoma of the prostate who, for the same reason of slow development of the primary focus, are relatively free from any symptoms of prostatism, but because of symptoms dependant upon the metastases naturally seek relief in other branches of medicine than urology. Metastases from a focus of carcinoma in the prostate not infrequently occur in the bones, particularly in the spine, producing cord symptoms and neuralgic and rheumatic pains dependent

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upon nerve pressure in various parts of the body, and particularly from pressure within the pelvis, producing symptoms of sciatica, are most common, and carcinoma of the prostate, as an explanation of such symptoms in adult males, should always be considered even in the absence of any symptoms of prostatic obstruction.

The difficulty in dealing successfully with carcinoma of the prostate surgically is, therefore, dependent chiefly upon the fact of the relatively rapid dissemination of metastases, so that by the time the patient develops the symptoms of prostatic obstruction a wide-spread metastasis has already taken place. This remarkable disproportion between the secondary manifestations of the condition and the primary focus leads to only a late recognition of the disease in most instances.

The benefits to be derived from surgery in carcinoma of the prostate are, briefly speaking, the relief of prostatic obstruction whereby the bladder is permitted to empty itself of its residual urine and the kidneys thus relieved of back pressure. Without this relief death is hastened by renal impairment, and it is my belief that more patients with unrelieved carcinoma of the prostate die from uremia than from the disease *per se*, and it is the symptoms dependent upon the condition in the urinary tract that contribute largely to the individual's suffering.

From the diagnostic standpoint there are certain subjective symptoms and objective findings which, in many instances, may differentiate carcinoma of the prostate from benign hypertrophy. Without entering upon a discussion of the pathology of the disease an explanation of the subjective symptoms is to be found in the fact that the primary focus in the prostate produces early metastases in the pelvic nodes, resulting in sciatic nerve pressure and giving the usual symptoms of sciatica. This disturbance is a common one, and, in fact not infrequently the most pronounced symptoms regarding which the patient complains. With such pain radiating to one or both sciatic regions, there is often an associated sacral and groin pain, all of which subjective symptoms should excite suspicion of malignant disease of the prostate, with pelvic metastases.

Bumpus (*ibid.*), recording the statistical data at the Mayo Clinic, notes that the first symptoms in seventy-nine patients with clinically demonstrable metastases was pain in 34%, while in 283 patients without clinically demonstrable metastases pain was the first symptom in but 12.01%; which strongly suggests that when pain of the character already referred to is a prominent symptom, pronounced metastases have, in all likelihood, already occurred.

Objectively, the sense of marked induration, loss of resiliency and irregular hard areas within the gland, as noted by rectal palpation, and especially if the induration extends upward onto the posterior surface of the bladder toward the seminal vesicles, in a prostate little or much enlarged, is characteristic of carcinoma of the gland, and is in contrast to the smooth, resilent, more or less rounded topography of benign hypertrophy. The only condition of the prostate with which carcinoma in the gland can be confused, is the small fibrous prostate or when there exists localized areas of greater density due to chronic inflammation, and in most instances the train of subjective symptoms already alluded to are wanting.

In the preoperative examination as well as in the histology, there are two types of carcinoma of the prostate. One, the most common, is the gland enlarged in varying degree with irregularities of almost stony hardness in the early stages of the disease, or after the whole gland has

become more or less involved in the infiltration, a general enlarged hard mass extending laterally toward the pelvic bones, and upward in the direction of the seminal vesicles, in which direction it has a tendency to spread. This is the type of carcinoma of the prostate which gives the greatest degree of urinary symptoms, because of obstruction. The other type, the most malignant, producing rapid and extensive metastases, shows but relatively little enlargement of the gland by rectal palpation, and the outline is uniform rather than irregular, but there remains the sense of firmness or even hardness. This type of carcinoma of the prostate is rapidly infiltrating in character, having little tendency toward localization. It produces a condition of the gland by rectal palpation which is most likely to be passed unrecognized, not only because of the lesser degree of urinary obstruction, but because it may readily be mistaken for an obstructing gland, providing obstruction exists, of the small, fibrous type or the changes produced by chronic inflammation.

It can be readily appreciated that those particularly alert in appreciating the differentiation referred to between a malignant and benign prostate will have a smaller degree of error in the recognition of the condition before operation; yet there remains a percentage of errors in the experience of the most expert, and those who operate much upon the prostate encounter, during the operation, the difficulty of enucleation or gross changes in the removed gland, which leads to a suspicion of the true condition. Such suspicion requires an immediate frozen section if possible, and if the gland is carcinomatous or any suspicion exists regarding this point, radium should be implanted in the prostatic region, as will be referred to later. There remains, further, a certain percentage of prostates which are carcinomatous, which will pass at operation as benign, the true condition only being realized by the pathological report. Too much emphasis cannot be placed upon the importance of the pathological examination of all prostates removed for this reason, and because a recognition of the condition calls for the postoperative treatment with radium, if we are to do everything to prevent a local recurrence of the disease.

If, during the preoperative examination, a condition in the gland is discovered which excites suspicion of carcinoma, a complete x-ray examination of the whole skeleton should be made, as bone metastases, both osteoplastic and osteoclastic, are not uncommon. Their presence may be entirely lacking symptomatically, for as Recklinghausen (*F. von. Die fibrocse oder deformèrende Ostitis, die Osteomalacie und die Osteoplastische Carcinose, in ihren gegenseitgen Beziehungen. Festschr.*, Virchow, Berlin, 1891, 1-89), has pointed out, the metastatic process in bone begins in the medullary portion. This evidence of bone metastasis I have found to be not an uncommon accompaniment to the disease, both ante mortem and post mortem, and which condition I will illustrate later by slides. Almost any bone may be involved, as shown by Carlier and Davrinche (*Les metastases osseuses dans le cancer de la prostate. Echo med, du Nord,* 1903, VII, 313-322) the vertebrae, pelvis, ribs and femur being the most common. Bumpus (*ibid.*), recording the Mayo Clinic cases shows in 135 patients x-rayed; metastases in the pelvis bones, 37.5 per cent.; spine, 35.8 per cent.; femur, 31.2 percent, and ribs, 6.9 per cent. While the presence of metastases may not be demonstrated by x-ray in the abdominal nodes and organs, their presence in the lungs is so portrayed not uncommonly, which fact is another argument for a complete roentgenological examination prior to operation; for with a

general metastasis without urinary symptoms, the patient may be better treated palliatively, or if operated upon because of urinary obstruction, for the purpose of prognosis and better understanding of the remote symptoms, which may develop.

The local urinary disturbances produced by carcinoma of the prostate are briefly those of benign prostatic obstruction. There is an impression that hematuria is more frequently associated with carcinoma of the prostate than with benign hypertrophy; with which I differ, for in my experience hematuria is far more common with a benign than with a malignant condition of the gland. The features of urinalysis are common to both conditions, but renal obstruction, with renal dilatation and pyelonephrosis, has occurred in a higher percentage with carcinoma than with benign hypertrophy, an explanation of which is to be found, I believe, dependent upon the pressure of involved pelvic nodes upon the ureter, which condition I have noted post mortem in several instances.

The usual preoperative study, cystoscopy, renal function tests and blood chemistry, determine the renal condition, and should be employed with prostatic obstruction due to carcinoma, as in benign hypertrophy, for by such means information of the patient's condition, both local and general, is obtained. In this connection the phenolsulphonephthalein test should be employed both intravenously and intramuscularly, for by the variation in the result of the test by both methods, important data may be had in estimating, in some measure at least, the patient's general condition, and together with other information of the patient's physical status, determine whether the patient should be treated palliatively or by radical means.

It would be an absolute misstatement of fact to assert any views other than considering carcinoma of the prostate as an inevitably fatal disease, yet it is likewise true that much may be accomplished in relieving the distress due to urinary obstruction both by palliative as well as by radical local treatment. If one contrasts the suffering due to the urinary obstruction with that dependent upon the metastases, there is no question that the individual, freed of his urinary difficulties and ill-being dependent upon renal impairment, lives the remainder of his life in relative comfort, and it is in that respect that any procedure that tends to ameliorate their suffering, even though it offer but little chance of permanent cure, should be employed.

I am convinced from my own, as well as the experience of others, that much may be accomplished along these lines; especially by the combination of surgery with radium therapy by choice, when the individual's condition permits, or by palliative measures by radium alone, or combined with bladder drainage when radical surgery is out of the question.

It is generally admitted that the suffering dependent upon urinary retention and the train of general symptoms dependent upon renal retention and infection, influencing the general condition, must be relieved. Prior to the advent of radium therapy prostatic carcinoma was treated surgically, with two ends in view. One method was palliative and the other an attempt at radical cure. The palliative method consisted of regular catheterization when possible, and permanent suprapubic drainage when necessary. An attempt was made to remove the gland either suprapubically or perineally by enucleation, curetting, or cauterization, to relieve obstruction. The radical method first advocated in 1882

by Leisrink (Leisrink, *Arch. f. Klin, Chir.,* 1882. Berlin, xxviii, 578) was to remove the gland with its sheath and unite the divided ends of the vesical neck with the membranous urethra by suture. A somewhat similar procedure was carried out by Fuller in 1898 (Fuller, *Journal of Cutaneous & G.-U. Diseases,* 1898, p 581), and in 1904 Young (*Johns Hopkins Bulletin,* Oct. 1905) modified the Leisink operation to include the seminal vesicles in the operation.

Both the palliative and radical methods relieved bladder retention and lessened, in consequence, the suffering dependent upon it; but the radical attempts did little more, for then, as now, the disease cannot be expected to be recognized prior to the development of metastases, so that any removal of the local growth did not accomplish a cure. It is today generally admitted that the radical operation as a curative means, is futile because, even with a complete removal of the local disease, the metastasis remains.

During the past five years radium has been quite extensively employed in certain centers of this country in various ways for the treatment of the disease under consideration. As yet no one method has been generally adopted. It is fair only to say that the use of radium by all the methods possesses merit, and favorable local results are obtained when employed independently or together with surgery. After personally observing from time to time the work of others who have concentrated upon this form of treatment, and from a lesser personal experience, I am convinced that it has much value, chiefly in preventing local recurrences if employed before and at the time of operation, and subsequently employed following the operative convalescence. Of this I have no question, and I believe that the day is not far distant when radium will be quite generally a part of the equipment on the instrument table when a prostatectomy is undertaken by those frequently performing the operation; for I feel sure that one doing many prostatectomies will admit that they are occasionally confronted with a carcinomatous gland which they considered to be benign prior to operation, and because the result, so far as local recurrence is concerned, is generally admitted to be better if radium is implanted in the prostatic region following the removal of all the gland tissue that can be removed surgically.

At a recent meeting of the American Association of Genito-Urinary Surgeons (*Trans. Am. Assoc. of G.-U. Surg., May,* 1921) a symposium on the treatment of carcinoma of the prostate brought out many viewpoints regarding the manner of handling the malady. In general the opinion could be classified into two groups, some contending that surgical procedures dealing with the malignant gland tended to favor metastases by opening channels for dissemination, and advocated treating the growth by radium alone, producing bladder drainage, if necessary, suprapubically. Others believe in removing as much of the malignant gland as possible, some by the suprapubic and some by the perineal route, with the implantation of radium in the prostate area, and subsequently treating the patient by local radium application. Favorable local results were recorded by both methods, but neither group presented evidence upon which could be formulated a general basis of treatment for all patients.

Reviewing my own cases prior to the employment of radium in connection with the treatment, it is found that the patient simply given permanent suprapubic drainage, had a less operative mortality and lives slightly longer, on the average, than those from whom the malignant

gland was removed. The former group has the inconvenience of a permanent suprapubic tube, and the latter were symptomatically relieved, but often had a local recurrence; and some, for this reason, required subsequently a permanent suprapubic drainage. It is a noteworthy fact, however, that there were a surprising number entirely free from the symptoms of prostatic obstruction by even an incomplete removal of the malignant gland, and were left to die in relative comfort from their metastases, or intercurrent diseases, which are the inevitable result in any event, but without a disturbing local recurrence. Since employing radium prior to and at the time of operation and carrying on subsequent radium treatment following operation, local recurrences have not been a disturbing factor. Moreover, in the treatment by radium of local recurrences in patients who did not have radiation at the time of operation, the radium has, I believe, in many instances taken care of the recurrence so that a permanent suprapubic drainage has been averted. Some of the patients were operated upon by other surgeons and only the recurrences have been observed by me; yet I am convinced that these patients were on the way to a permanent suprapubic drainage, except for the benefits received from the local radium treatment.

Those who have had the greatest experience in connection with radium treatment without surgery are Barringer, at the Memorial Hospital in New York, Young of Baltimore, and the Mayo Clinic. One should not receive the idea that the policy of treatment at these clinics is adverse to operation, for they are not; but they have had an extensive experience in connection with treating the condition by radium without operation. There is a group of patients having obviously a carcinoma of the prostate who have been subjected to treatment without operative interference chiefly for the reason that they either have relatively slight symptoms of prostatic obstruction or because metastases are so advanced that operation other than permanent suprapubic drainage would be fatal.

Personally, I have come to classify patients with carcinoma of the prostate into two broad groups. One, in whom an attempt may be made to relieve the prostatic obstruction because of much residual urine, and eradicate the disease locally by removing as much of the gland as possible, even including the seminal vesicles and prostatic sheath in certain instances, and leaving radium in the prostatic area for from 500 to 1000 millicurie hours, according to how much of the growth is left at the time of operation, and subsequently, about three weeks later, giving daily radium treatments through the rectum, urethra, and bladder for a period of about thirty days, giving 100 millicurie hours at each treatment.

The operation, if undertaken, I believe, is preferably done through the perineum, essentially according to the technique of Proust (*Comptes rendus de l'Assoc. Francaise d'Urologie*, 1901.) The patients falling into this class are those with symptoms dependent upon prostatic obstruction and those whose general condition will permit of such surgical intervention as proven by the usual method of preoperative study generally employed in prostatic patients.

The other class includes patients with disturbing symptoms of prostatic obstruction and whose general condition is not up to the required standard for the radical operation. They may be subjected, in some instances, to the so-called "Punch" operation, with subsequent radium

treatment, or subjected to a suprapubic drainage and treated with radium by introducing needles containing radium into the gland through the suprapubic opening, at the time that it is established, and leaving the radium needles implanted in the gland for from 500 to 1000 millicurie hours, and subsequently treating the malignant gland by radium therapy through the rectum, urethra and bladder, as previously mentioned.

A few months ago I had the opportunity of operating upon a patient who originally had marked prostatic obstruction from a malignant gland, which was removed by Dr. Hugh Young in January, 1921, with radium left in the prostatic region, and who received subsequently radium treatment as previously outlined. In June, 1921, he came under my care with a deep urethral stricture and large, foul residual urine. Through a perineal incision I was able to investigate the prostatic area and remove tissue from this region. There was no gross evidence of carcinoma and the histology of the removed tissue showed it to be fibrous tissue only. I believe that in this instance the local malignant disease had been eradicated. While this is the only patient that has permitted of an investigation of this sort, there are others who are free from urinary obstruction following the procedure referred to, and by all non-operative methods of investigation are locally free from the disease.

The other class, which is a large group, includes patients with few distressing symptoms of prostatic obstruction and those with recurrence of the disease locally, following operation. This group is subjected to radium treatment alone, or combined with regular catheterization and irrigation, if necessary, to relieve a residual urine or bladder infection.

The radium treatment which I have adopted in this group is a combination of the methods employed by Barringer (*Trans. Amer. Assoc. Gen.-Urin. Surg., June,* 1921) and by Young (Jour. Urology, Vol. 1, No. 6, Dec., 1917.)

The Barringer method is the introduction of metal needles containing radium or radium emanation, fixed on a shaft not unlike a small trochar, into the gland through the perineum. For this purpose four 12½ milligram needles may be employed at the same time, placing them in different portions of the gland and also into the seminal vesicles, if desired, guiding their introduction with a finger in the rectum while they are being introduced into the desired areas through the perineum. The needles, having been placed, are left from 300 to 1,000 millicurie hours. This procedure requires that the patient remain in bed, there is usually little if any reaction, but urinary retention requiring not more than a few catheterizations has occurred occasionally.

While Barringer is content, through a large experience, to leave these patients, without further radium treatment, for several weeks, when they are again needled, if it seems advisable, I have preferred to supplement the needling by a course of treatment by the method employed by Young, about three weeks after the needling. The treatments consist in making daily applications of radium for 100 millicurie hours by means of a special instrument introduced into the prostatic region through the rectum, urethra, and transvesically; in the ratio of usually three rectal to two urethral to one bladder application, varying the method of application according to circumstances, and never applying the radium to the same area on successive days because the susceptibility of the mucous membrane of these different avenues of application is

subject to considerable individual variation, and irritation from the radium may develop if care is not taken in this respect. At the end of this course of treatment the gland, and if advisable the seminal visicles, are again needled by the Barringer method, and the course of treatment for the time being is ended.

These patients should be examined in about a month, and according to the changes in the condition depends the decision as to further treatment. During this interval catheterization and bladder lavage may be carried out if necessary.

The results have proven conclusively, to my mind at least, that radium employed by the Barringer or Young method has a striking beneficial result, as I have reason to know from observing their work from time to time prior to employing it myself. My decision to combine the two methods was not from failure on their part, but rather to employ every means of attacking the disease. Recently Young has adopted the needling method to supplement his form of treatment for the same reason, applying the needles, as a rule, at the end of the course of rectal, urethral and bladder applications.

The course of treatment as outlined is essentially that employed at the Mayo Clinic also, and in a recent personal investigation of their results, I find that they classify them briefly into (1) those relieved of all symptoms, (2) the growth shrinks, but some urinary obstruction remains, (3) in some there is no change, and (4) that there are some remarkable results and apparently local cures. In a recent personal investigation of the results of Young's Clinic at the Brady Urological Institute, I find that they classify their results as follows: (1) actual beneficial results, which means diminution in size and softening of the carcinomatous gland with relief of retention in most instances; (2) symptomatically improved, meaning diminution in frequency of urination in about 60 per cent., relief of local pain in over 70 per cent., the cessation of bleeding in all cases where it was a factor; and about five per cent. of patients have gone over four years without return of local symptoms, and are apparently local cures.

My own experience, by no means so extensive, substantiates in substance these results, with some reservations. There have been several patients with local recurrence following operation who, without employing radium at the time of operation, have, through treatment by radium as outlined, shown such improvement in the size of the growth and obstructive symptoms, that, in my opinion, they have been relieved of the necessity of producing a permanent suprapubic drainage. It should be mentioned that the relief of symptoms and diminution in the size of the gland must not be expected to take place during the course of radium treatment, and several weeks must pass before favorable results can be expected; and even then all that may be desired and hoped for may not take place, with the result that another course of treatment may have to be instituted. There have been some patients in whom the gland has softened and diminished much in size, yet some retention remains and all symptoms have not disappeared.

On the whole, however, the patients are symptomatically and locally improved, and there are some with apparently local cures.

The mental attitude of the patient with carcinoma is a feature familiar to us all, and one has been much impressed with the new hope, false perhaps, that has come through the unqualified popular expressions as to the wonders of radium, which, after all, is no small individual

matter when one has been led to believe that nothing further can be done after the operation has failed. It is fortunate that we are in possession of such data as to be able to give such patients some hope founded on fact.

On the other hand, the history of the subject shows conclusively that carcinoma of the prostate is an inevitably fatal disease occurring from three general causes: local urinary obstruction with renal impairment and infection; metastases; and inviting intercurrent diseases from lowered general resistance. When all is said and done, all we can accomplish in this disease is to relieve the local condition either by operation, combined with radium therapy in certain instances, or by radium therapy alone, which, however, is no small accomplishment when such procedure tends to ameliorate suffering even though it offers a very small chance of permanent cure.

METHOD FOR THE INTRODUCTION OF RADIUM NEEDLES INTO TUMORS OF THE BLADDER.

By JOHN H. CUNNINGHAM, M. D., Boston, Mass

It being a well established fact that malignant tumors are much more efficaciously treated by the insertion of radium into the tumor mass than by surface applications, the device here described has been made and satisfactorily employed in the treatment of malignant tumors of the urinary bladder. With the exception of a special device to implant radium emanation into tumors of the bladder all other instruments employed for radium treatment of malignant tumors of the urinary bladder, by way of the urethra, have been employed for the purpose of applying radium to the surface of the tumor mass rather than within its substance.

In developing the present instrument there has been a desire to avoid making a special cystoscope for the purpose of implanting the radium within the tumor. Instead, the new device can be used through the Brown-Beurger operating cystoscope, as are the other instruments commonly employed with this instrument.

The device itself (Fig. 1) consists of a solid metal block mounted on a flexible shaft, similar to the shaft employed in other cystoscopic operating instruments. Into this metal block are screwed two radium

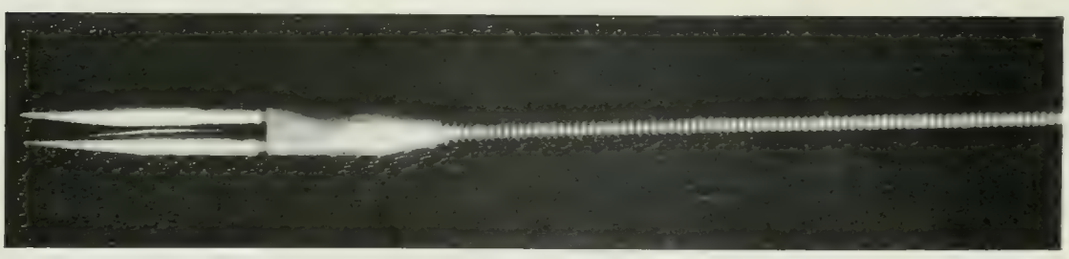

Fig. 1.—Shows radium needles (also employed for internal radiation of carcinoma of the prostate), screwed into the metal block mounted on the flexible shaft.

needles which contain amounts of radium up to 15 milligrams; the same type of needle as employed in the internal radiation of carcinoma of the prostate, so that the needles employed for one may be employed for the other purpose. The device constitutes a small fork which may be plunged into the tumor mass through the Brown-Beurger operating cystoscope (Fig. 2 and Fig. 3), and the cystoscope "fixed" by the employment of a "mechanical hand." The "mechanical hand" already on the market and pictured in Dr. Hugh Young's article (Technique of Radium Treatment of Cancer of the Prostate and Seminal Vesicles; Surgery, Gynecology and Obstetrics; January, 1922; page 93), being most satisfactory for the purpose.

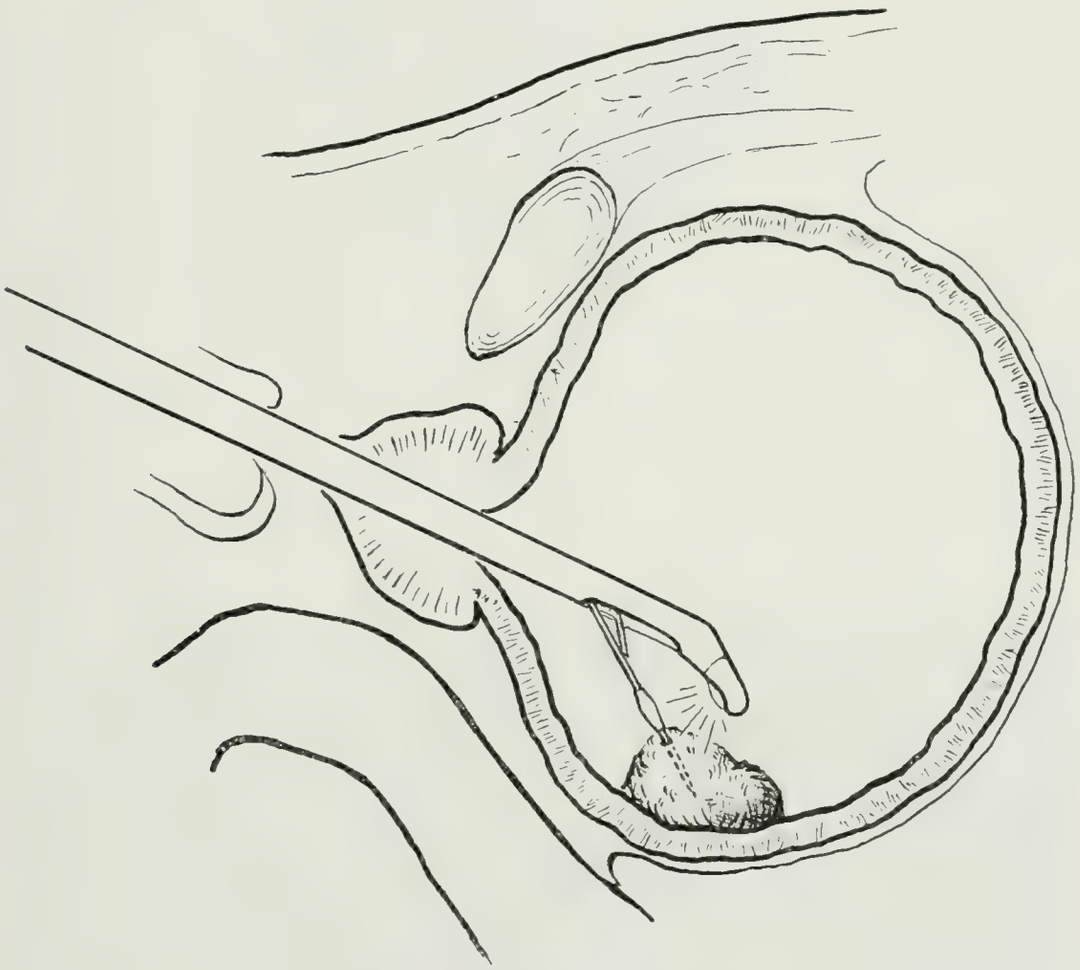

Fig. 2.—Shows a diagramatic cystoscopic picture of the radium needles inserted into a tumor mass.

The technique of application of the new device differs but little from that employed in connection with the various cystoscopic operating instruments, the only different feature being that the radium device is too large to be passed through the cystoscope while the optical tube is in position. For that reason, following the irrigation of the bladder through the irrigating sheath, the radium instrument must first be passed through the irrigating sheath and guided out of the cystoscope into the bladder by previously introducing the flexible metal guide (Fig. 4-A)

along which the radium device is passed. The flexible shaft is then threaded onto the optical tube as it is passed into the irrigating shaft. The bladder is thus distended and the radium needles manipulated in the manner similar to any of the operating cystoscopic instruments (Fig. 4-B.)

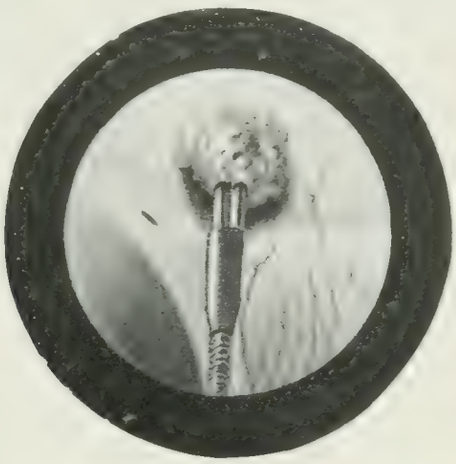

Fig. 3.—Shows diagramatically the radium needles inserted into the tumor mass.

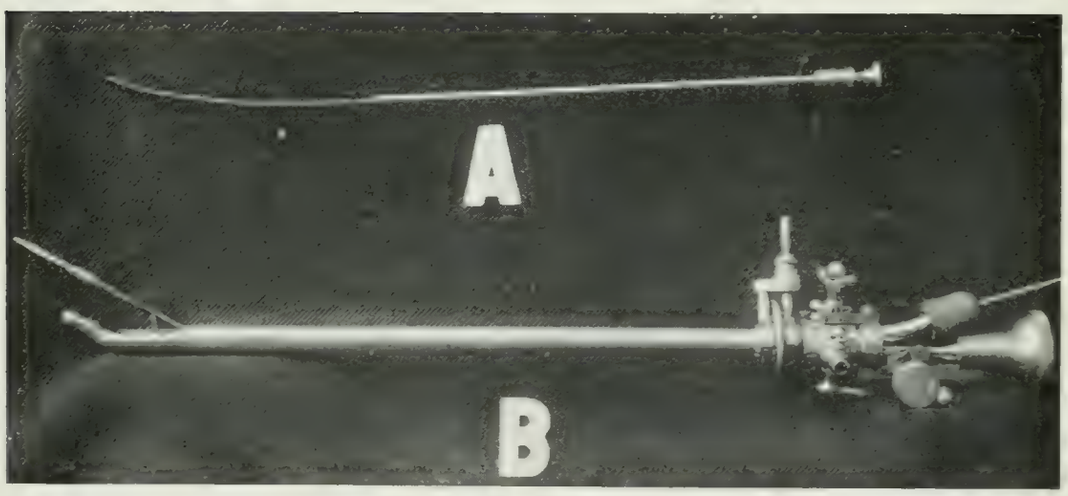

Fig. 4.—A shows the flexible metal shaft employed to guide the radium device out of the cystoscope into the bladder. B, the Brown-Buerger operating cystoscope with the radium device in position.

TECHNIQUE OF RADIUM TREATMENT OF CANCER OF THE PROSTATE AND SEMINAL VESICLES*

By Hugh H. Young, M.D., F.A.C.S., Baltimore

From the James Buchanan Brady Urological Institute, Johns Hopkins Hospital

At the International Medical Congress, London, 1913, in the Section of Urology, Pasteau and Degrais presented a method for the treatment of cancer of the prostate with radium. The technique consisted simply in introducing a silver tube containing radium to which was attached a long wire which was employed to introduce the radium into the catheter to the proper distance, into the urethra, where it was left in place for an appropriate length of time. In Figure 1 the catheter with radium in place is shown schematically. Being impressed with the good results which Pasteau had secured in two cases by this extremely crude apparatus, I secured 102 milligrams of radium element in a glass tube and set about to construct more accurate instruments for the introduction of radium into the urethra, prostate, and rectum. The first instruments employed were provided with a straight cystoscope, the same cystoscope which I had used for several years in the construction of my cystoscopic rongeur (Fig. 2). With this cystoscope as a basis, the instrument shown in Figure 3 was made, and it at once became possible to introduce radium not only into the urethra and rectum, but into the bladder where, under cystoscopic direction, it could be applied to the region desired. It became evident at once that some means of firmly fixing and holding the instrument containing the radium was necessary in order to keep the application against the desired area for the entire period of treatment. Casting about for an instrument, I made use of the cystoscopic clamp or artificial hand which I had employed for several years to hold a photographic cystoscope in place during exposure of the plates. A ball of appropriate size was then placed around the shaft of the radium applicator which, when firmly grasped by the cystoscopic clamp, held the radium instrument in its grasp upon the desired spot. The completed instrument is shown in Figures 3 and 4. This then was the basis for a series of instruments which have since been constructed, the object of which has been to place radium upon a certain spot under the direction of either the cystoscope in the bladder or a finger in the rectum and to hold it there during the entire treatment seance.

It soon became evident that it was not necessary to use the cystoscope for applications of radium in the urethra or at the vesical orifice or even against the trigone, as it is easily possible by simple manipulation to determine where the instrument is in its relation to the vesical neck or to place the radium exactly where it is desired and then hold it there with the clamp. For the rectum the cystoscopic instrument was manifestly not necessary as the radium containing beak could easily be placed at the desired spot along the posterior surface of the prostate or vesicles or along the pelvic wall and held there by the clamp. We, therefore, constructed instruments of appropriate form not containing cystoscopes

*Reprinted by permission from Surgery, Gynecology and Obstetrics, xxxiv, 93-98, January, 1922.

for treatment through the rectum, urethra, at the vesical neck or through the trigone and base of the bladder to the region of of the seminal vesicles.

Figure 5 shows the present form of instrument which is employed for these treatments. The radium is contained in a small platinum tube

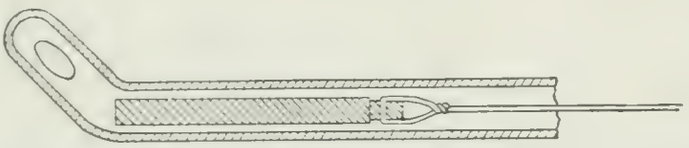

Fig. 1.—Catheter method of Pasteau and Degrais for applying radium in cancer of the bladder and prostate.

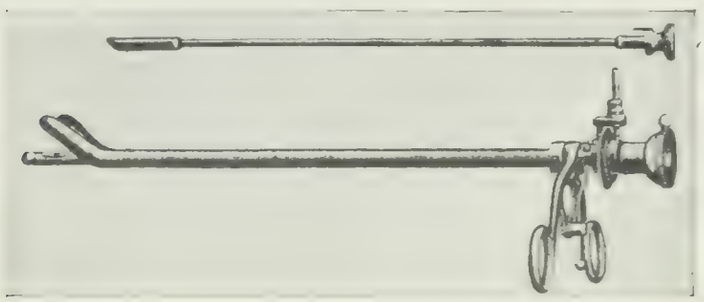

Fig. 2.—Author's cystoscopic rongeur for obtaining sections of vesical tumors for microscopic study.

Fig. 3.—Author's cystoscopic radium instrument 1 carrying a tube of radium in fenestrated platinum capsule in beak; closed with obturator.

Fig. 4.—Instrument 1 with straight cysotscope introduced.

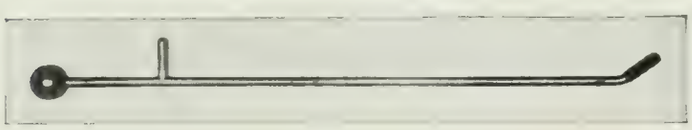

Fig. 5.—Rectal radium carrier, applied under direction of index finger in rectum, and held in place by mechanical hand or clamp.

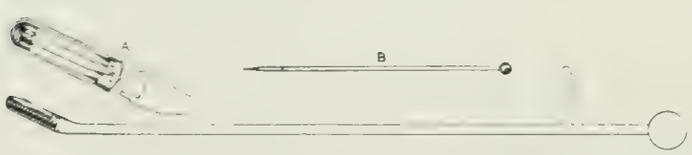

Fig. 6.—New radium applicator with enlarged cap, a, made to contain four needles containing 12½ milligrams of radium each, which may be used also for needling through the perineum by means of attachable shaft, b.

which is surrounded by a metal cap covered with hard rubber, thus affording screening for both the alpha and beta rays, and also the secondary rays. The ball is placed at the end of the rod thus facilitating usage in both rectum, urethra and bladder, the small handle at right angles to the shaft facilitates operation, and indicates the direction of the beak.

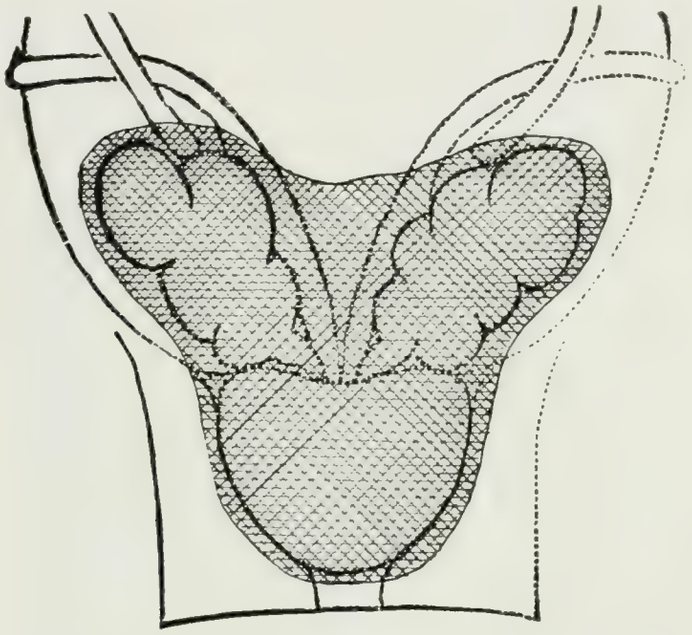

Fig. 7.—A typical chart of carcinoma of prostate and seminal vesicles.

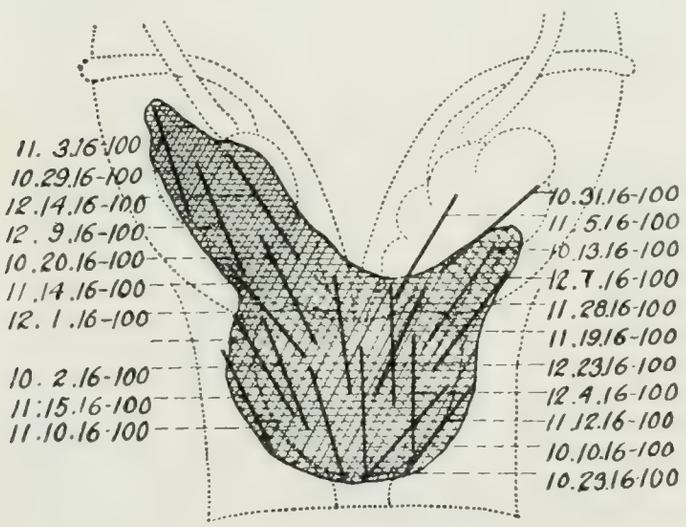

Fig. 8.—A case of cancer of the prostate and left seminal vesicle (right vesicle slightly involved). The radium treatments, each representing 100 milligram hours, are shown and date of each is recorded.

Recently since the introduction by Barringer of the needling method for the treatment of carcinoma of the prostate through the perineum, I have made up in the workshop of the Brady Urological Institute an instrument which contains within the beak four needle points each containing 12½ milligrams of radium surrounded by a cap of silver which is surrounded by gutta percha. This instrument was supplied to and is in use by Dr. John H. Cunningham of Boston. Figure 6b shows the needle with shaft attached for insertion through the perineum.

Technique Employed. In the preliminary study of the cases a careful diagram showing the size and consistence of the prostate is made, utilizing a rubber stamp outline of normal prostate and vesicles as a basis. In making the examination with the finger of the left hand, the outline chart is drawn simultaneously, careful attention being made to get an accurate reproduction of the size and induration of the mass. The degree of induration is indicated on a scale of four, blank being normal, parallel lines, slight induration; cross lines moderate induration, and additional cross lines (at 45° to the other two parallel lines) great induration, such as is characteristic of carcinoma. A typical chart of carcinoma of the prostate and seminal vesicles is shown in Figure 7.

If the diagnosis is clear from the extreme induration of a portion of the prostate and the absence of calculus from the x-ray examination,

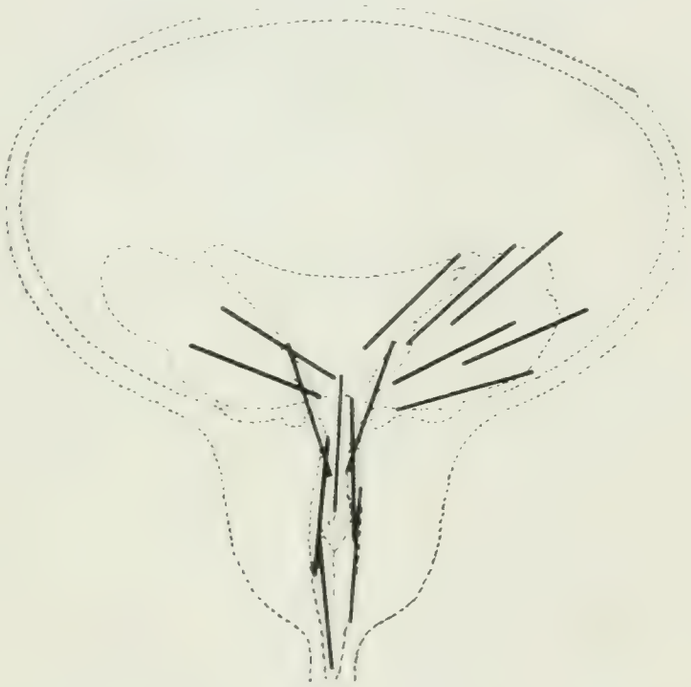

Fig. 9.—Chart showing the transvesical and transurethral treatments given in each case illustrated in Figure 8. Each line represents 100 milligram hours.

a cystoscopic examination may not be carried out. As a rule cystoscopy is much more painful in cases of carcinoma than in cases of hypertrophy, and if it is not necessary for diagnosis we usually do not insist on cystoscopy. If there is a question as to the diagnosis, cystocopy is performed and is of diagnostic importance, first, because in cases where hypertrophy is present, the prostatic orifice usually shows no intravesical lobes or enlargement more than a small median bar or minute rounded lobe, and, second, because there is shown by examining with the finger in the rectum and cystoscope in the urethra a markeod increase in the suburethral portion of the prostate, not merely in the prespermatic or subcervical group of glands, but also beneath the entire prostatic urethra from the vesical orifice to the apex, and this increase in the suburethral portion of the prostate is usually associated with marked induration. This is based on the pathological fact that prostatic hypertrophy almost never involves the so-called posterior lobe which lies between the posterior capsule and the ejaculatory ducts above and the lower portion of the prostatic urethra below, and that the same region

is strangely the point of predilection for carcinoma. This diagnostic sign was first pointed out by me 16 years ago, and has been of great value in the diagnosis of early and doubtful cases.

The diagnosis of carcinoma having been made, the question arises as to whether a radical operation can be carried out with the proba-

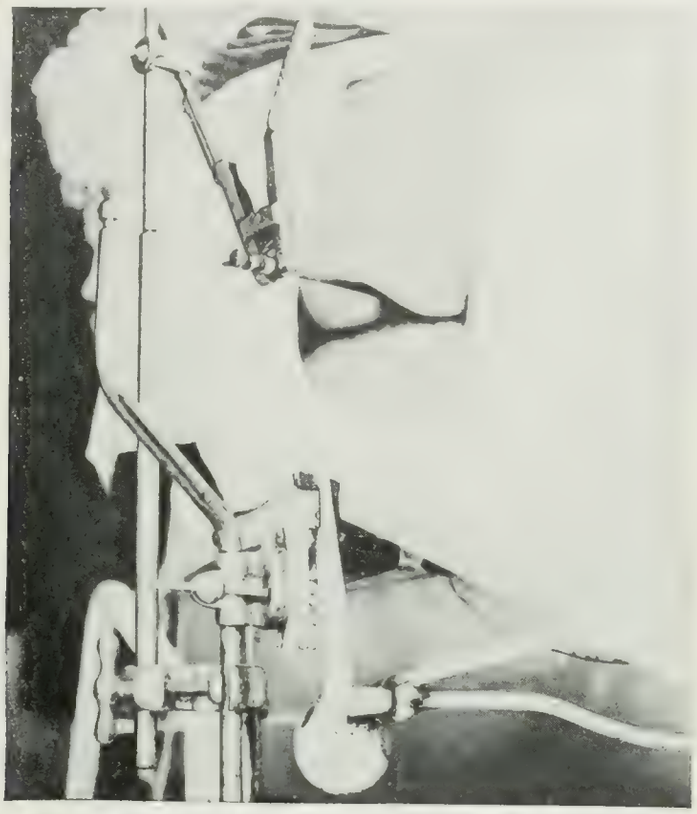

Fig. 10.—Mechanical hand in use in treating cancer of seminal vesicles and prostate through rectum.

Fig. 11.—Mechanical hand or clamp holding radium instrument in position desired.

bility of success. We have now had sixteen cases in which we have carried out our radical technique, and are able to report over 50 per cent. apparent cures followed over a period of 5 years or more, and in

the last four cases by a modification of technique, through which the preprostatic vessels, nerves, and fascia are preserved intact, complete urinary continence has been obtained.

Fig. 12.—Radium needles being applied. Finger in rectum, determining course and position of needle.

Fig. 13.—Sagittal section to show finger in rectum and position of radium needle.

Experience has shown that in cases in which the carcinoma is confined well within the capsule of the prostate, in which it has involved only the lower portion of one or both seminal vesicles, and in which it

has not penetrated the prostatic capsule or fascia of Denonvilliers which covers not only the prostate but the seminal vesicles, the radical technique can be carried out with strong probability of a complete cure and a good functioning bladder with perfect control and without urethral stricture at the site of anastomosis.

Unfortunately, the great majority of cases present themselves much too late, the disease has already progressed well up along the sides of the seminal vesicles, and frequently involves the lower pelvic glands, only forming a plateau of marked induration above the prostate in the intervesicular region. In many of these cases there is no marked urin-

Fig. 14.—Radium needles in position.

ary disturbance beyond a slight residual and some increased frequency, owing to the fact that carcinoma of the prostate tends to invade the structures above, behind the bladder, and does not penetrate or ulcerate until later into the urethra or bladder. On this account operative relief for the obstruction is usually not necessary, and one is free to choose methods of attack upon the carcinoma which is usually producing symptoms due to its size and pressure upon nerves and adjacent structures. The plan of procedure for thorough treatment with radium which was first proposed by me before the American Urological Association at its meeting in Baltimore, 1915, and subsequently presented in a paper (1) has been carried out in over one hundred cases, the results of which will be presented in an accompanying paper by Dr. Clyde L. Deming, resident urologist of the Brady Urological Institute.

In my first paper, Figures 8 and 9, the charts of cases were presented in which 100 milligrams of radium was applied for one hour

each by rectum, urethra and bladder to various positions. In one such case it was given twenty-one times through the rectum and fourteen times through the urethra and bladder as shown in Figures 10 and 11. The only modification which has been made in the past 4 years has been to employ an instrument, the beak of which is protected by a gutta percha cap, scrupulous care being taken to avoid applying radium twice in the same place, generally the successive treatments being given to places quite remote from each other, and alternating between the rectum, urethra and bladder. Before the introduction of these methods it was freely stated that it was impossible to employ radium in sufficient dosage through the rectum without producing radium burns. By means of this technique, in which the radium is placed in position with the finger in the rectum and held there by the cystoscopic clamp, care being taken to avoid regions that have already been treated until 2 or 3 weeks have elapsed, radium burns and even pronounced irritation have been practically eliminated, so that we now find it possible to give with impunity twenty treatments, 1 hour each, through the rectum with 100 milligrams properly screened in the small applicator above described. The treatments through the urethra (which furnishes at least four or five separate and isolated positions), and through the trigone and lateral portions of the base of the bladder, are of very great importance as only the mucous membrane and submucous tissues separate the radium from the carcinomatous prostate or vesicles. Since the introduction of Barringer's needles, we have added this method of treatment to our routine technique, and now employ two needles at a seance, each of which, containing 12½ milligrams, is inserted through the skin of the perineum (which has been cocanized) into one or both prostatic lobes or even into the carcinomatous mass above the prostate or along the lateral wall of the pelvis in the region of the seminal vesicles (Figs. 12, 13 and 14). These needles are allowed to remain in place for a period varying from 18 to 24 hours. They are introduced under the direction of a finger in the rectum (which should not be covered with glove or finger cot in order to be acutely sensitive to the exact position of the needle). This procedure should be repeated three or four times during the first series of treatments and adds a valuable amount of radiation to the central portions of the prostate and seminal vesicles where it is most remote from the radium applied through urethra, bladder, or rectum. As at present given, one complete series consists of an hourly treatment of 100 milligrams of radium properly screened and applied with the special applicator alternately 20 times through the rectum, 10 times through the urethra, and 10 times through the trigone and also 12½ milligrams 8 times through the perineum. As noted before in these regions there is sufficient area to provide for treatments which do not overlap or repeat at the same spot and therefore do not produce ulcerations. With such a series of treatments most amazing resorption of extensive carcinomatous involvement of prostate and seminal vesicles and tissue adjacent to them is obtained in the majority of cases and along with it there comes a disappearance of pain and obstruction, a return usually to more normal urination and freedom from straining which is indeed remarkable. Figure 10 shows radium applied through the rectum with patient upon his side and the clamp in operation. Figure 11 shows the instrument in place for treatment of the urethra or bladder.

Recently I have constructed an applicator which carries in the beak two tubes of radium, 100 milligrams each, placed end to end and thor-

oughly screened with 2 millimeters of platinum and a thin layer of gutta percha. This materially shortens the treatment as 200 milligram hours is given each hour with this applicator instead of 100 milligram hours.

Details of Treatment. Before mounting the table patient should empty bladder, and if necessary evacuate bowels. For treatments through the rectum no anæsthesia is necessary. For the urethra and bladder it is well to inject 4 per cent. procaine before introduction of radium applicator. In very painful cases it may be desirable to give a sixth of a grain of morphine or opium suppository one-half hour before treatment. In some cases treatments can be given twice a day, but usually the patient objects and one treatment of 1 hour each day is all he will take. We usually alternate between urethra, rectum and bladder, picking each time an invaded region which has not been previously treated. The record of treatment is made upon either the prostatic or urethral and bladder chart, as shown in the accompanying cases. A line is drawn showing exactly where the radium was applied and the date is indicated on the line which points to the site of application. The treatments through the perineum with needles is indicated in a similar way upon a third chart, thus the entire treatment is recorded simply upon one page, and the operator can determine at once the location to be treated next in order to avoid overlapping and consequent burning. Another series of rectal charts, four in number, are made two weeks apart. These show the progress of the case and often demonstrate remarkable disappearance of extensive infiltration and induration, as shown in some of the cases charted below. The subject of results, however, will be left to Dr. Clyde L. Deming, who will present a careful study of over one hundred cases. It is necessary to explain that during the period of the war the vigorous attack which had been outlined in our first paper was not carried out, and many of the cases in which Dr. Deming is forced to report received inadequate treatment but they may be used to show the imperfect results obtained by insufficient treatment and to be contrasted with those which have been thoroughly radiated, according to the method above outlined. In a certain proportion of cases, probably 10 per cent., obstruction persists, and the presence of residual urine and frequent urination necessitated operative removal of the obstruction. In these cases I have pursued a plan which I have employed in carcinoma of the prostate (associated with hypertrophy or with great obstruction) since 1905, viz., conservative perineal prostatectomy with enucleation of the obstructing median and lateral lobes and careful preservation of the urethra and ejaculatory ducts. Almost invariably the patient is given as thorough a treatment as possible with radium through the rectum, urethra, and bladder before the prostatectomy is carried out. During this course of radium treatment in most cases the obstruction disappears, but in others operation is necessary and the results obtained are generally functionally as good as in benign hypertrophies. In some cases radium is introduced into the prostatic cavities at operation, but care must be taken to protect the rectum by sponges and rubber protective which hold the radium sufficiently far away from the rectum.*

*In a recent case of carcinoma of the prostate and right seminal vesicle, I first made a perineal incision and exposed the posterior surface of prostate and vesicles as in perineal prostatectomy (without opening the urethra) and then introduced bare tubes of radium emanation. 1 mc. in amount, 1 cm. apart. No difficulty was experienced in implanting the tubes over the entire area of induration, and also well above the vesicles. This method would seem to furnish a very accurate method for radical treatment with radium.

RESUME.—In conclusion it may be said that by the technique which we have above outlined really remarkable results are often obtained in apparently incurable and very extensive cases of carcinoma of the prostate and seminal vesicles. Extraordinary functional results are sometimes obtained with relief of pain, hæmaturia, difficulty and frequency of urination, and attending discomforts. In some cases apparently radical cures have been obtained, but time is yet too short to pronounce definitely upon this point. Suffice it to say that in a desperate class of cases, a great boon can often be furnished and their remaining months or years at least made far more comfortable.

REFERENCES

1. The use of radium in cancer of the prostate and bladder, a presentation of new instruments and new methods of use. J. Am. Ass., 1917, lxviii, 1174.

2. Young, Hugh H., and Frontz, W. A. Some new methods in the treatment of carcinoma of the lower genito-urinary tract. J. Urol., 1917, i, 6.

3. Young, Hugh H. The use of radium and the punch operation in desperate cases of enlarged prostate. Ann. Surg. 1917, May.

RESULTS IN ONE HUNDRED CASES OF CANCER OF PROSTATE AND SEMINAL VESICLES, TREATED WITH RADIUM*

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1. Results of Radium Treatment in 100 Cases of Cancer of Prostate and Seminal Vesicles.

By the use of surgical, internal and autoserum therapy, science has failed thus far to produce satisfactory results in the treatment of extensive carcinoma of the prostate. As a consequence, medicine has turned its attention in another direction, namely to the use of radium. Many institutions have been using radium for a number of years, and now private physicians are tempting its healing qualities. The many details of this treatment are by no means well understood as indicated by the different forms of radium used, the amounts used, and the large number of instruments invented for its application. Yet, the world having been aroused by the great possibilities of the gamma rays, is anxiously awaiting results concerning the cure of this fatal disease. Like the surgical results for cancer, so with the results of radium we must be content to wait a reasonable length of time before a cure can be definitely determined. Prostatic cancer is one of the slowest growing malignancies, and even after a lapse of 4 or 5 years after treatment, we may not be justified in pronouncing a cure. Hence, we must expect results will be given with a great deal of caution. However, we feel that

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the time limit is past and we are apprehensive to receive the results which have already been obtained.

The paper by Dr. Hugh H. Young on "Technique of Radium Treatment for Cancer of the Prostate and Seminal Vesicles" shows an evolution in the technique of applying this means of treatment which has been devised by him at the James Buchanan Brady Urological Institute. The growth of this therapy, like the development of many medical problems has profited by its mistakes. The results during such progression must be expected to show variation. This paper shows the results obtained at the Brady Institute in 100 cases of prostatic cancer treated with radium.

The statistics extend over the war period during which time the great care and precision of treatment could not be carried out. Some cases were receiving too large doses at one sitting, while others were receiving too frequent treatments in the same area, and still others were receiving inadequate doses. All cases included in this series were patients with advanced and extensive cancer who were considered beyond the operable stage.

The study of incidence of these 100 cases shows that the youngest to develop such an advanced type of cancer was 45 years and the oldest was 84 years. The largest percentage of cases is found in the seventh decade which includes 45 per cent. Thirty-five per cent .occur after this decade and 80 per cent. after the sixtieth year.

TABLE I.—AGE ON ADMISSION FOR TREATMENT

NO. OF CASES	YEAR	PERCENTAGE	DECADE
3	45th to 50th	3	Fifth
17	51st to 60th	17	Sixth
45	61st to 70th	45	Seventh
25	71st to 80th	25	Eighth
10	81st	10	Ninth

The diagnosis of cancer was made in all cases by rectal examination. All cases presented the same physical findings as did 175 others which were operated on in this clinic, and all proved microscopically to be cancer. The prostate was enlarged, broad, irregular, nodular, fixed, and stony hard. The seminal vesicles, when invaded, were found broad, flat, indurated, forming an intravesicular plateau. In many of the cases lymph glands were palpated along the lateral walls of the pelvis. The seminal vesicles were involved in 90 per cent. of the cases. The membranous urethra was invaded in 51 per cent. It was broad, hard, firm, and in some cases presented a tubular-like growth. The rectal wall was invaded in 15 per cent. of cases. No ulcerations were found in the rectal mucosa. All cases then were typical of extensive cancer growth.

The amount of radium used varied greatly, ranging from 300 to 6225 milligram hours, the average being 1600 milligram hours, but this average is no criterion for ideal results as will be shown later in this paper. The radium was given in courses or series extending over a period of 4 to 6 weeks after which there was an interval of rest for 2 to 3 months when the second series was given. The largest number received only a single series, while a few receivd as many as five series extending over a period of 2 years.

The treatments were administered per rectum, per urethram, and per vesicam, and a combination of these as described by Dr. H. H. Young

(1). Fifteen received rectal treatments alone, three urethral alone, and one intravesical alone. Fifty received a combination of rectal and urethral, 26 a combination of rectal, urethral, and intravesical; 3 rectal and intravesical; 2 urethral and intravesical—in all 99 received rectal treatments, 83 urethral, and 31 intravesical.

Results. In studying the results of radium treatment of carcinoma of the prostate, we find that they naturally fall into four groups: (1) *Symptomatic and functional,* where the frequency, dysuria, hæmaturia, dribbling, and the size and force of the stream have improved or returned to normal; (2) *local,* where there is a change in the size and consistence of the prostate and seminal vesicles; (3) *good* results or lasting results after 4 years of complete subsidence of all the symptoms, and where the prostate and seminal vesicles no longer present the characteristics of malignancy, but are soft and elastic; (4) those cases which showed no relief of symptoms and no actual change in the prostate and seminal vesicles.

Symptomatic and Functional

Symptomatically, the results from radium have been most remarkable. Seventy-seven per cent. of the cases show a relief of some or all of the symptoms. Patients who have been suffering from marked frequency, occurring every 10 to 60 minutes day and night, others who have hesitancy and pace the floor only to void very small amounts of bloody urine with a much diminished stream, and still others who have constant pain in the back and thighs, have been completely relieved. Striking are the results in those cases who have had a suprapubic cystotomy for relief of complete obstruction, when, after a series of treatments, the wound spontaneously healed and the patient gradually developed a normal act of micturition. The mental anxiety associated with these cases must not be forgotten. Many of the patients resume their normal mental status and gain weight and strength after a course of treatment.

Haematuria. Blood in the urine was present in 17 per cent. of the cases. This was due to the extension of the tumor through the bladder or urethra. Radium applied to these surfaces caused an immediate cessation of bleeding similar to application of radium to the surfaces of bladder tumors or to the cancer of the cervix. All of the cases responded within a week or 10 days or after two to four treatments.

No. 4977 was a patient aged 68 who had haematuria for 6 months. The bleeding was present at each urination but varied its appearance, occurring sometimes at the beginning and sometimes at the ending of urination. Rectal examination proved the cancer to involve the posterior half of the prostate and the whole of both seminal vesicles. Cystoscopy showed the cancer breaking through the trigone. On March 24, 1916, 100 milligrams of radium were applied to the right side of the trigone and 50 milligrams to the left side. On March 27, 100 milligrams were applied to the left side. All treatments were given intravesically. The patient was next seen on April 3. Haematuria had entirely subsided. Patient lived for one year, dying of general carcinomatosis, although he received a total of 2900 milligram hours of radium. He never had a recurrence of blood in the urine and lived a comfortable life except for pain in back during the last 2 weeks of life. Such is the record of those complaining of haematuria. All of them responded immediately to the treatment and were permanently relieved.

Complete retention. Complete obstruction to urination was noted in 17 cases. (Several of these cases were able to pass a few drops of urine, perhaps an ounce in 24 hours). They were being catheterized regularly by themselves or by physicians. Catheterization was painful in most of

the cases as they had a marked cystitis together with urethritis. The urethra in these cases is unlike that seen in benign prostatic hypertrophy cases in which the urethræ are encroached upon by large, soft and elastic lobes, causing potentially enlarged urethræ, while in the carcinoma cases the caliber of the urethræ is smaller than normal. It is firm and rigid due to the infiltration of the suburethral tissues by the tumor. Radium in these cases has produced remarkable results. Fifteen of them began to void after twelve or fourteen treatments. Seven were completely relieved of residual urine, while 8 showed a diminution which varied from 10 to 50 cubic centimeters. Two were unable to void after 2100 milligram hours. These two were obstructed due to benign median lobes. Where there is much hypertrophy, the result of radium on obstruction and residual is not so pronounced.

No. 5445 was admitted with complete retention. He was 80 years of age. History of urinary symptoms dated over a period of 2 years. He had residual urine of 400 cubic centimeters. The prostate was considerably larger than normal, irregular, indurated, and stony hard. The right seminal vesicle was corded, irregular, and adherent. The left seminal vesicle was an inch broad, flat, indurated, and extended upward as far as the finger could reach. There was an intervesicular plateau. The membranous urethra was obscured by adhesions and by the low position of the prostate which was invaded by the tumor. There were no enlarged glands felt. The rectum was smooth and moved freely over it. Radium was applied, 600 milligram hours in the urethra, and 200 milligram hours intravesically in a period of 6 weeks. Two weeks after the beginning of treatment the patient voided small amounts of urine. At the end of the series, patient was voiding all his urine. Urinations occurred every 3 to 4 hours without hesitancy, urgency, or dysuria. The size and force of the stream was almost normal. Rectal examination at this time showed great reduction in the area of induration in both the prostate and seminal vesicles, and one would not recognize the condition as one of carcinoma. The patient's urinary condition returned to normal and remained normal for 4 years. His general condition improved and he gained 15 pounds in weight. Patient has not been examined for 2 years but replies to questionnaire that he voids every 3 to 4 hours without difficulty.

Still more remarkable are those cases which have had a suprapubic cystostomy for complete retention. Radium applied in these cases produces a restoration of urination through the urethra with a good-sized stream and complete control together with healing of the suprapubic wound.

No. 7684 had a month previous to admission a suprapubic cystostomy for complete retention. All the urine was draining through this wound. After a series of radium treatment extending over a period of 6 weeks, the wound was entirely healed and the patient voided with a good-sized stream every 3 hours. No. 8271 had had 6 weeks previously a suprapubic drainage for complete obstruction due to carcinoma of the prostate and seminal vesicles. After receiving 700 milligram hours per rectum, 300 milligram hours per urethram, and 800 milligram hours per vesicam, patient was able to void naturally. Urinations occurred every 3 hours during the day and every 4 hours at night. The wound closed and the patient gained 25 pounds during the next 3 months. No. 8719 had a perineal prostatectomy 2 years previous to admission and 6 months later the wound opened and began to discharge urine. Examination showed that he had an extensive carcinoma of the prostate, seminal vesicles, and urethra. After 6 weeks of treatment, during which time he received 2700 milligram hours of radium, 1800 per rectum, 500 per urethram, and 400 per vesicam, the fistula closed and he voided freely through the urethra.

Residual urine. Sixty-six cases had residual urine, varying from 50 cubic centimeters to 700 cubic centimeters. About the third week of radium treatment, the size and force of the stream began to increase and the residual urine gradually became less. Eighty-five per cent. of the 66 cases were entirely relieved and were able to empty their bladders

completely. Thirteen per cent. showed a diminished residual, while 2 per cent. did not show any change. No. 7521 had 400 cubic centimeters residual urine on admission. After 6 weeks of radium treatment, during which time 1400 milligram hours were given, the residual urine had entirely disappeared and patient was voiding with ease. Since 60 per cent. of the cancer cases had an infected urine, the relief of this residual adds greatly to the comfort of the patient and likewise removes the great possibility of a septic process supervening a malignancy.

TABLE II.—IMPROVEMENT IN SYMPTOMS

Before Treatment		Result of Treatment		
Symptoms	Percentage Present	Percentage Entirely Relieved	Percentage Improved	Percentage Unimproved
Frequency	96	57	25	18
Nycturia	95	57	25	18
Dysuria	80	90	—	10
Hæmaturia	17	100	—	—
Hesitancy	65	80	7	13
Dribbling	76	75	5	20
Small stream	87	74	6	20
Complete retention	21	95	—	5
Residual urine	61	85	12	3
Pain in back	28	60.7	—	39.3
Pain in extremities	22	59	—	41
Loss of weight	14	57.1	—	42.9

Hesitancy. Delay in starting the urinary stream was noted in 65 cases. In 80 per cent. of these it cleared up completely; 7 per cent. were improved, and 13 per cent. remained uninfluenced by the radium rays.

Dribbling. Seventy-six patients gave a history of dribbling of the urine either at the beginning, during, or at the end of urination. In 75 per cent. of these this symptom entirely subsided, while 5 per cent. were improved and 20 per cent. remained unaffected.

Size and force of stream. There was a larger percentage of cases who showed an impairment in the size and force of the urinary stream. While many of these patients had dribbling, there were some who had only a diminished size of stream and voided with little force. The statistics show that 87 per cent. voided with much diminished size and force of stream. The effect of radium is practically the same as that on dribbling (75 per cent. relief). The relief of this symptom is one of the earliest signs of improvement. Usually after 10 to 12 treatments, there is a notable difference with regard to the ease with which the stream starts and the force with which it flows. Both improve gradually, the maximum time limit for improvement being about 6 to 8 weeks after the termination of the treatment.

Frequency and nycturia. Frequency is one of the first symptoms to appear in cancer of the prostate. It was the most common symptom to be noted in the 100 histories. Frequency and nycturia were present in 96 per cent. and 95 per cent. respectively. There are, of course, many degrees of frequency, but in this classification are included all cases who voided oftener than 3 hours. Some of the more severe cases

voided every 5 to 10 minutes. Fifty-seven per cent. of the cases were cured of this frequency. In this group are classed all those patients who, after treatment, voided not oftener than every 4 hours during the day and who were able to retain urine at night 8 hours without discomfort. Twenty-five per cent. were improved so that they voided not more frequently than every 2 to 3 hours during the day and did not have to get up more than twice at night. Eighteen per cent. did not show any improvement. Some patients showing reaction to radium began to void less frequently after the third week and continued to improve, while others did not show any improvement until after the series had ended. This can be explained from our study of sections of prostates which have been removed at operation at different intervals after radium treatment. During the first 2 weeks there is considerable œdema of the tissues, especially of the parenchyma, and then there is a gradual change to fibrosis and a disappearance of the cancer cells. When the fibrous change begins, there is a shrinking of the tissues with the result of dominished pressure on the urethra and internal vesical orifice. We have noticed in a few cases an increase of frequency for a few days. This period of exaggeration of symptoms corresponds to the œdematous stage of the tissues.

No. 6759 was admitted with frequency every 30 to 60 minutes day and night. The patient received 1300 milligram hours per rectum and 200 per urethram. Three months after beginning of the treatment he was able to retain urine for 6 to 10 hours and voided with a normal-sized stream.

No. 8718 had on admission a frequency of every hour day and night. In 7 weeks he had 2700 milligram hours of radium, 500 to the urethra, 400 intravesically, and 1800 to the rectum. He had slight increase for the first weeks and then the intervals between urination began to lengthen, and after 2½ months he was voiding at normal intervals.

Dysuria. Pain in the form of strangury was generally relieved after a few treatments. Burning and smarting in the posterior urethra and neck of the bladder also were greatly ameliorated. Eighty per cent. of the cases complained of painful urinations. Ninety per cent. of these were free from pain after the first series. The 10 per cent. who failed to respond all received small amounts of radium, less than 1200 milligram hours. The dysuria usually subsided when the size of the stream increased. Some of the cases were very much improved after five treatments. It is impossible to explain so early a result due to radium. It is feasible, however, to believe that passage of cystoscope or the radium applicator might cause a dilatation of the urethra and the improvement of the act of urination. But the greater part of the result came during the fourth and fifth weeks when the rectal examination showed a softening of the prostatic tissues.

No. 6759 complained of severe burning, hesitancy, dysuria, dribbling, and frequency of every hour day and night on admission, March 2, 1916. On April 6 he had very slight irritation in the neck of the bladder which lasted until May 1. During this time he had received 1800 milligram hours of radium. Patient could then hold urine 6 hours during the day and for 10 hours during the night, and voided with natural ease.

Pain in the back and extremities. Dull aching pain in the small of the back was noted in 28 per cent. of the cases. This pain was present day and night, regardless of position. It never radiated to the shoulders; it either was stationary or was referred down the thighs, especially on the outer side. Sixty and seven-tenths per cent. of these cases reported an entire relief of the pain. The remainder were very little, if any, improved. X-rays were taken of most of the cases. About

65 per cent. of the patients who complained of pain in the back showed metastases. The fact that metastases were present did not appear to influence the effect of radium locally.

No. 8493 was admitted complaining of pain in back, right hip and groin. Nineteen hundred milligram hours of radium were given, 1100 per rectum and 800 per urethram, in 8 weeks. X-ray showed bones of pelvis, especially both ilia, to have evidence of general metastatic carcinoma. The bones were thickened and roughened. The lumbar vertebrae showed a marked thickening of the spine. Pain never disappeared entirely but was ameliorated, and the patient was fairly comfortable and did not require morphia. He voided every three hours during the day and every four hours at night.

In most cases pains in the extremities were described as an aching sensation, weakness, like a hot iron passing over the thighs and like flesh being pulled from the bones. They were mostly referred to the outer side but rarely to the inner side of the thighs; always to the muscles and never to the joints. Extremity pains were present in 22 per cent. of the cases. Fifty-nine per cent. of these responded to treatment, while 41 per cent. showed no improvement. The improvement is probably due to resorption of the infiltration which involved nerves in the lower pelvis.

TABLE III.—CASES RECEIVING ONLY 1 SERIES OF RADIUM

No.	Milligram Hour	Frequency	Duration of Series	Symptoms Imp'ved	Local Improvem't	Irritation
1	1000	2-d	3-w	+	+	—
2	550	2-d	2-w	—	—	—
3	800	3-d	2-w	+	+	+
4	1050	2-d	4-w	++	—	—
5	1200	2-d	3-w	—	—	—
6	1100	2-d	3-w	—	—	—
7	1100	3-d	4-w	+	—	—
8	1300	2-d	4-w	+ —	—	—
9	800	3-d	4-w	+	—	—
10	2600	2-d	7-w	+ + —	+ + +	—
11	500	2-d	10-d	—	—	—
12	1000	3-d	4-w	—	—	—
13	600	2-d	3-w	—	—	—
14	600	2-d	10-d	—	—	—
15	600	2-d	2-w	—	—	—
16	850	3-d	4-w	—	—	—
17	250	3-d	10-d	—	—	—
18	800	3-d	3-w	—	—	—
19	400	2-d	1-w	—	—	—
20	800	3-d	3-w	—	—	—
21	1300	3-d	6-w	—	—	—
22	1600	3-d	7-w	++		—
23	1400	2-d	4-w	—	—	—
24	1900	3-d	8-w	+ + +	—	—
25	450	5-d	2-w	—	—	—
26	700	7-d	4-w	—	—	—
27	420	1-d	1-d	—	—	—
28	400	2-d	2-d	—	—	—
29	200	1-d	1-d		—	—
30	1050	7-d	6-w	—	+	—
31	400	5-d	2-w	+	—	—

TABLE III.—CASES RECEIVING ONLY 1 SERIES OF RADIUM

No.	Milligram Hour	Frequency	Duration of Series	Symptoms Imp'ved	Local Improvem't	Irritation
32	700	14-d	6-w	+	—	—
33	865	14-d	4-w	—	—	—
34	200	1-d	1-d	—	—	—
35	1700	6-d	8-w	+++	++	—
36	1300	2-d	6-w	++	—	—
37	1525	4-d	6-w	++	—	—
38	2050	3-d	7-w	+++	++	—
39	700	3-d	3-w	+	—	—
40	1850	2-d	8-w	+	+	—
41	2500	2-d	8-w	++	++	+
42	309	1-d	1-d	—	—	—
43	400	2-d	8-d	+	—	—
44	420	7-d	4-w	+	—	—
45	330	7-d	1-w	—	—	—
46	1800	3-d	7-w	++	+	+
47	1200	2-d	4-w	+	—	+
48	2100	3-d	8-w	+++	++	+
49	1315	2-d	4-w	++	+	—
50	1625	14-d	9-w	++	+	—
51	1445	3-d	6-w	++	—	—
52	1500	3-d	6-w	—	—	+
53	2975	3-d	8-w	+++	++	—
54	2100	3-d	8-w	++	++	—
55	1000	3-d	4-w	+	—	+
56	600	2-d	2-w	—	—	—
57	900	3-d	4-w	+	—	+
58	2800	3-d	7-w	+++	+++	+
59	800	3-d	3-w	+	—	—
60	400	2-d	1-w	—	—	—
61	700	2-d	2-w	+	—	—
62	900	2-d	3-w	+	—	—
63	700	3-d	3-w	—	—	—
64	1000	3-d	4-w	+	—	—
65	1200	4-d	7-w	+	—	—
65	....	...	...	39	16	11
65	1045	3-d	4-w	60%	23%	17%

Note: d = day.
2-d = treatments given every 2 days.
3-4 and 4-d = treatments given every 3 and 4 days.

Loss of weight. Fourteen patients complained of loss of weight, ranging from 10 to 50 pounds. Most of the patients were professional men and sought relief before the picture of cancer was implanted on their external features, so that the marked anæmia, emaciation, and cachexia were rarely seen. The general health of most of the patients improved after radium treatment. Appetite returned to normal and the general physical condition became distinctly elevated. Fourteen of the cases gained weight varying from 8 to 25 pounds. The feeling of better-

ment usually began about the second week and continued, depending on the symptomatic result. Some patients continued to lose weight and strength, especially those who were in later stages of the disease with signs of metastases in groins or elsewhere.

Local Results. The local result of radium on prostatic cancer is expressed by a change in the consistence and diminution in the size of the prostate and seminal vesicles. While the local results are not so remarkable as the symptomatic, the examining finger detects a most gratifying condition. Since the evolution of treatments has undergone many changes in technique, one would expect a variation of results which is readily borne out in the tabulations.

In 55 of the 100 cases a marked change in the size and consistence was demonstrated. The hard stony-like character was changed to a much less indurated tissue with a definite elasticity. The prostate itself became normal in size and the vesicles smaller and movable. The hard plateau gradually disappeared, leaving a sensation of a chronic inflammatory condition. The hard nodules when present in these cases melted away. The palpable glands along the side of the pelvis became indistinct and non-palpable.

TABLE IV.—SIXTY-FIVE CASES RECEIVING ONLY 1 SERIES OF TREATMENTS.

No. Cases	Symptoms	Size of Prostate	Ave. Milligram Hrs.	Percentage Improved	Percentage not Imp'ved
26	no response	no change	625	0	100
39	improved	no change	999	60	40
16	improved	decreased	1415	23	77

No. 5818 showed on admission a very large, adherent, irregular, nodular, stony-hard prostate with the prostate with the process extending upward and involving the seminal vesicles. There was also a definite fixation of the prostate with the formation of an intervesicular plateau. The patient received in 2 months 2400 milligram hours per rectum and 400 per urethram, making a total of 2800 milligram hours. At the end of the series the prostate was normal in size, adherent, and chronically inflamed. There was nothing to suggest malignancy. The stony character had entirely disappeared; fixation of the structures was replaced by a definite degree of mobility. Some of the cases showed a subsidence of the hard character without a diminution in the size of the mass.

A number of these cases were operated upon and found to be benign hypertrophies coexistent with carcinoma. The radium usually affected the cancer tissue, but failed to produce any marked change in the benign hypertrophy.

The cases showing local result were given 1000 to 6225 milligram hours of radium. One to five series were administered over a period of 6 weeks to 2 years. Thirty-one cases received only one series of treatment and averaged 2300 milligram hours. Eleven received 2 series averaging 2500 milligram hours; 6 received 3 series, averaging 2900 milligram hours; 5 received 4 series, averaging 3000 milligram hours; and 2 cases received 5 series, 5227 milligram hours and 6225 milligram hours respectively. Many of these treatments were given 1 to 3 days apart with an interval of several months between series. Doubtless

much better results might have been obtained had the more recent technique of treatment that is now in vogue been carried out.

The changes in the tissue occur usually about the third to the fifth week. This change can be detected shortly after the onset of symptomatic improvement. Cases vary to some degree on this point, but as a rule it can be detected near the end of the first series. Cases which had seminal vesicle involvement showed similar changes, provided radium was directed over them. It was formerly thought difficult to obtain changes in the vesicles, but it is now known that the treatments were not accurately given in these regions. A great deal can be accomplished by placing the radium intravesically over the seminal vesicles as well as high up in the rectum.

Tables III and IV show result in those cases receiving a single series of treatments. It will be readily seen that those cases which showed no response to radium received the smallest amount, while those which showed a symptomatic improvement received a larger amount and those which showed local effect or a change in the size of the tumor received a still larger amount. It is apparent that more radium is required to produce a demonstrable change in the carcinoma than to affect the symptomatology. Table IV does not indicate the degree of improvement of the symptoms and change in the prostate; for none of them received enough radium to produce a complete subsidence of all the symptoms or complete resorption of the cancer tissue.

Table IX shows that the greater the number of series the greater was the percentage of local improvement. The average amount of radium was progressive as the series advanced and it was not until 3000 milligram hours were given that the cases showed a 100 per cent. symptomatic and local improvement. This amount does not necessarily mean that these patients have been cured, as different patients react differently and no two show the same status of cancer involvement. All cases receiving this amount showed some degree of improvement in symptomatic and in the local condition.

Five Cases Showing Good Results

There were a few cases which apparently responded to radium in a remarkable manner. The immediate results were excellent. They were entirely free from symptoms and rectal examination showed regression of the tumor so that the prostate was normal in size. These patients have enjoyed apparently perfect health for 4 years; two have had a recurrence of symptoms and three remain perfectly well after this interval. The amount of radiation has been large in all these cases.

TABLE V.—CASES RECEIVING 2 SERIES OF RADIUM

No.	First Series		Interval	Second Series		Total		Results		
	Milligram Hours	Duration		Milligram Hours	Duration	Milligram Hours	Duration	Symptoms	Local	Irritation
1	2000	1-w	1-w	780	1-w	2780	2.5-m	+++	++	+ sl.
2	2600	5-w	12-w	2000	10-w	1600	6 -m	+++	+++	+ sl.
3	1050	4-w	2-w	675	1-w	1725	2 -m	—	—	—
4	2100	3-w	12-w	500	4-d	2600	1 -m	+++	++	+ sl.
5	750	3-w	2-w	900	2-w	1650	2 -m	+++	+	—
6	700	2-w	4-w	800	2-w	1500	2 -m	+	+	—
7	600	2-w	4-w	800	2-w	1400	2 -m	++	—	—
8	600	2-w	8-w	800	2-w	1400	3 -m	+	+	+
9	900	3-w	12-w	1200	4-w	2100	5 -m	—	—	—
10	300	3-d	12-w	500	5-d	800	3 -m	++	—	—
11	500	1-w	26-w	250	1-d	750	6.5-m	—	—	—
12	1200	3-w	12-w	700	2-w	1900	4.5-m	+	—	—
13	1600	3-w	8-w	500	10-d	2100	3 -m	+++	+	—
14	1000	3-w	12-w	500	5-d	1500	4 -m	++	+	—
15	900	3-w	12-w	500	2-w	1400	5 -m	—	—	—
16	1200	5-m	20-w	600	8-w	1800	12 -m	—	—	—
17	3070	5-m	16-w	2200	8-w	5270	10 -m	+++	+++	—
18	450	3-w	8-w	450	1-w	900	3.5-m	—	—	—
Averages	1248	4.1-w	10-w	786	2-w	2065	4.3-m	66.6	50.0	22.2

d=day. w=week. m=month. sl.=slight.

TABLE VI. CASES RECEIVING 3 SERIES OF RADIUM

No.	First Series		Interval	Second Series		Interval	Third Series		Total		Results		
	Milligram Hours	Duration		Milligram Hours	Duration		Milligram Hours	Duration	Milligram Hours	Duration	Symptoms	Local	Irritation
1	1200	3-w	5-w	400	2-w	7-w	500	4-w	2100	5-m	+++	+++	—
2	2160	6-w	6-w	885	1-w	3-w	265	1-d	3290	5-m	+++	+	+
3	725	2-w	10-d	1115	3-w	3-w	920	3-d	2760	3-m	+++	+++	+
4	1100	1-w	10-w	300	1-w	3-m	500	1-d	2290	7-m	++	—	+
5	1300	4-w	1-w	750	3-w	7-w	675	2-w	2725	4-m	+	++	—
6	1200	6-w	5-w	400	2-w	9-w	400	3-w	2000	6-m	—	—	—
7	800	12-d	4-w	600	8-d	6-m	600	10-d	2000	8-m	—	+	+
8	1800	4-w	6-w	900	3-w	6-w	400	8-d	3100	5-m	+	++	+
9	400	3-w	2-w	700	6-w	2-w	600	4-w	1700	5-m	—	+	—
10	1450	2-w	6-w	1100	3-w	4-m	400	3-d	3150	7-m	++	—	—
	1243	3.6-w	4.7-w	735	2.5-w	9.1-w	536	1.7-w	2503	5.6-m	70%	70%	50%

TABLE VII.—CASES RECEIVING 4 SERIES OF RADIUM

No.	First Series		Interval	Second Series		Interval	Third Series		Interval	Fourth Series		Total		Results		
	Milligram Hrs.	Duration		Milligram Hrs.	Duration		Milligram Hrs.	Duration		Milligram Hrs.	Duration	Milligram Hrs.	Duration	Symptoms	Local	Irritation
1	875	2-w	7-w	350	1-d	6-w	1135	10-d	3.5-yr.	700	1-w	3160	3 1/3-y.	++	+++	—
2	1460	4-w	3-w	700	2-w	2-w	960	4-w	2-m	200	2-d	3320	9-m	+++	+++	+
3	980	2-w	2-w	325	5-d	5-w	500	10-d	2-m	1100	3-w	2905	5-m	+++	+++	—
4	700	2-w	13-w	600	10-d	6-m	600	10-d	11-m	1800	6-w	3700	2-yr.	+++	++	+
5	700	2-w	5-m	300	5-d	4-m	600	2-w	12-m	500	8-d	2100	22-m	+++	++	± sl.
	943	2.5-w	9-w	455	5.6-d	2.5-m	759	2-w	15-m	860	2-2.w	3037	20-m	100%	100%	60%

TABLE VIII.—CASES RECEVING 5 SERIES OF RADIUM

No.	First Series		Inter-val	Second Series		Inter-val	Third Series		Inter-val	Fourth Series		Inter-val	Fifth Series		Total		Results		
	Mg. Hr.	Duration		Mg. Hr.	Duration		Mg. Hr.	Duration		Mg. Hr.	Duration		Mg. Hr.	Duration	Mg. Hr.	Duration	Symptoms	Local	Irritation
1	1100	1-w	3-w	1400	5-w	6-w	900	1-w	1-w	1550	1-w	6-w	1275	3-w	6225	8.5-m	+++	+++	±
2	1100	2-w	11-m	500	1-w	4-m	700	1-w	3-m	400	4-d	4-m	1000	2-w	3200	24-m	+++	++	±
	1100	3-w	6-m	850	3-w	2.7-m	800	2.5-m	2-m	975	2.5-w	2-7-m	1135	2.5-w	4712	16-m	100%	100%	100%

TABLE IX.—SUMMARY OF TABLES III, V, VI, VII AND VIII SHOWING RELATION OF AMOUNT OF RADIUM TO DEGREE OF IMPROVEMENT.

No. of Series	No. of Cases	Average Milligram Hours	Duration	Symptomatic Improvement					Local Improvement				
				Total Percentage	Percentage Degree				Total Percentage	Percentage Degree			
					+++	++	+	0		+++	++	+	0
1	65	1045	4-w	60.0	10.7	18.0	13.3	40.0	23.0	3.0	7.7	12.3	77.0
2	18	2065	4.3-m	66.6	33.3	16.6	16.6	33.3	47.6	11.1	11.1	27.4	52.4
3	10	2503	5.6-m	70.0	30.0	20.0	20.0	30.0	70.0	20.0	30.0	20.0	30.0
4	5	3037	20-m	100.0	80.0	20.0	0	0	100.0	60.0	40.0	0	0
5	2	4712	16-m	100.0	100.0	0	0	0	100.0	50.0	50.0	0	0

Note: +++ = complete subsidence of all symptoms or complete resorption of the tumor. ++ = moderate change + = slight change.

TABLE X.—CASES RECEIVING 1 SERIES OF TREATMENTS

Result	No. Cases	Ave. Milligram Hrs.
No response	23	625
Symptomatic alone	20	999
Symptomatic and local improvement	22	1415

Note: Symptomatic improvement was not complete in many of these cases, nor was there complete resorption of the cancer tissue.

TABLE XI.—EFFECT OF RADIUM ON LONGEVITY

Number of Cases.		Ave. length of life after onset of symptoms
Now dead	48	2.54 years
Not improving	13	3.60 years
Improving	12	4.40 years
Good	5	6.00 years
Unheard from	22	

(Radium treatments were begun in all cases from 1 to 2 years after onset of symptoms).

TABLE XII. EIGHTEEN CASES TREATED RECENTLY (NOT INCLUDED IN THE 100 CASES)

No.	Age	Frequency of Treatment	RADIUM							Results	
			Urethral	Vesical	Rectal	Interglandular (Needle)	Total	Duration	Irritation	Symptoms	Local
1	69	2-d	600	700	1300	.....	2600	6-w	slight	+ +	+ +
2	65	1-d	1000	100	1500	.....	2900	6-w	none	+ + +	+ +
3	67	1-d	450	400	1000	.....	1850	4-w	slight	+ +	+
4	73	1-d	500	400	1800	500	3200	6-w	none	+ + +	+ + +
5	78	1-d	800	900	2300	.....	4000	6-w	slight	+ + +	+ + +
6	62	1-d	500	400	1000	.....	1900	7-w	none	+ +	.....
7	63	1-d	800	300	1300	.....	2100	5-w	none	+ +	+
8	72	1-d	900	.....	2100	500	3500	7-w	none	+ +	+ +
9	80	1-d	500	100	1800	.....	2700	7-w	none	+ +	+ +
10	68	1-d	500	100	1900	.....	2800	5-w	none	+ + +	+ +
11	71	1-d	1100	850	2100	500	4500	6-w	slight	+ + +	+ + +
12	65	1-d	700	500	2700	500	4105	6-w	slight	+ + +	+ + +
13	64	1-d	900	500	2300	1000	4700	6-w	slight	+ + +	+ + +
14	68	1-d	900	400	2750	500	4500	6-w	slight	+ + +	+ + +
15	71	1-d	400	500	2300	1000	4200	6-w	slight	+ + +	+ + +
16	66	1-d	1100	900	2000	1000	5000	8-w	slight	+ + +	+ + +
17	62	1-d	800	800	2400	1000	5000	7-w	slight	+ + +	+ + +
18	69	1-d	500	600	3100	500	4700	7-w	slight	+ + +	+ + +

No. 5230, 72 years of age, was admitted June 21, 1916, complaining of difficult urination. History dated over a period of 3 to 4 years, beginning with frequency, hesitancy, and dysuria. The frequency had increased so that he was voiding about every hour. Dysuria was the dominating symptom. Six weeks before entry to the hospital complete retention occurred. On admission rectal examination showed a markedly enlarged prostate. It was smooth and elastic, although the impression given was that of an underlying markedly indurated posterior lobe which was malignant. The outlines of the prostate could not be distinctly made out. The mass extended well up on the left to the left wall of the pelvis and was densely indurated and adherent. The right lobe of the prostate was not so markedly enlarged. The right seminal vesicle was invaded in its lower portion, densely indurated and adherent. Along the outer portion of the left lobe there was a hard nodular area. The membranous urethra was involved in a mass of marked induration. The lower portion of the prostate and that part extending up over the left lobe was practically of stony hardness. The bladder wall above the upper confines of the prostate was soft and yielding. He was treated by retention catheter and given radium to the amount of 2050 milligram hours, 200 milligram hours of which were given through the urethra, the remainder of which was applied through the rectum during the following 8 weeks. At the end of 6 weeks the patient was voiding at rather frequent intervals but without pain. He was then given 200 milligram hours per urethram which caused a temporary obstruction. Rectal examination at the end of 8 weeks showed the mucosa of the rectum to be only slightly thickened. The prostate was very little larger than normal. The consistence was rather elastic and would impress one, feeling it for the first time, as a moderate grade of benign prostatic hypertrophy. The right lobe was a little more indurated than normal, particularly on the periphery. Otherwise, the consistence of the prostate showed nothing which indicated malignancy. The seminal vesicles were just palpable; they were soft and elastic. During the next year the patient gained 17 pounds and general health improved. Urinations took place every 3 or 4 hours. Four years later patient reported that he had begun to use catheter occasionally, voided every 2 to 3 hours, and had lost considerable weight and strength. Patient was examined at end of 3 years but not since. At that time there was no evidence of recurrence of the cancer.

No. 4726 had complete retention on admission to the hospital and after a course of radium enjoyed 4 years of perfect health, after which he had a recurrence of urinary symptoms. He was first admitted to the hospital on November 18, 1915. His history dated over a period of 1 year. He complained of frequency and hesitancy. Two weeks before entry to hospital he developed complete retention. Rectal examination showed prostate to be modrately enlarged, the median furrow and notch shallow. Pressure in the median line elicited induration and it was impossible to pass the finger between the lateral enlargements as usual. The right lobe was irregular, nodular, very hard, almost stony. The induration was more pronounced toward the apex and toward the lateral portion. The upper end was somewhat soft and elastic, thought a little irregular. The right seminal vesicle was slightly irregular, not enlarged, but moderately adherent externally, no nodules, and no marked tenderness. The induration of the prostate did not extend into the membranous urethra. The left seminal vesicle was slightly thickened, drawn outward, a little corded, and moderately indurated. One or two glands were palpable far out along the lateral wall of the pelvis. Between the two seminal vesicles the intervesicular space was soft, no indurated cords or glands. Rectum was negative. Cystoscopic examination showed slight intravesical hypertrophy of the right and left lobes of the prostate. The median portion was elevated in the shape of a bar without sulci on either side. There was no anterior cleft. The trigone was a little hypertrophied but the ureteral orifices were no closer to the prostatic orifice than normal, and the mucous membrane covering the ureteral ridges and trigone was smooth. With finger in rectum and cystoscope in the urethra, the beak was easily felt. The trigone was not thickened but the median portion of the prostate was considerably thicker than normal and quite firm. The patient was given 80 milligram hours per rectum, 785 milligram hours intravesically, and 1000 milligram hours per urethram in 3 months. During this time he had gained 20 pounds in weight. Urinations occurred every 2½ hours during the day and night without any difficulty. Rectal examination revealed a condition simulating chronic prostatitis. The left lobe was

slightly irregular. The right was similar to the left. The right seminal vesicle was far less indurated than is often seen in a seminal vesiculitis. The left seminal vesicle was slightly larger than the right but of the same consistence. Six months after the beginning of the treatment, the prostate was found to be slightly broader than normal, but there was no area in the prostate or vesicles characteristic of malignancy.

The patient reported 5 years later stating he had enjoyed the best of health, had not suffered any pain or difficulty in urination except at times when there was a little hesitancy. Recently he had had to get up 3 to 4 times at night to urinate. Rectal examination showed prostate to be quite prominent, moderately enlarged, surface slightly irregular, extremely hard. Induration extended up on each side and involved the lower portion of the seminal vesicles and formed a definite intervesicular plateau. There were no enlarged glands felt and the rectum was perfectly smooth.

This patient received only 2635 milligram hours of radium. Had he received over 4000 in a shorter period, say 8 weeks to 2 months he might have been cured.

No. 5193 was admitted June 14, 1916 complaining of frequency of urination and difficulty in starting the stream. Three years previously he began to urinate every 2 hours day and night. Frequency increased to every hour, associated with dribbling and difficulty in beginning urination. Rectal examination showed prostate and seminal vesicles involved in a definite carcinoma. The prostate itself was only moderately enlarged and a little more prominent than normal. Median furrow and notch were shallow. The right lobe was irregular, considerably indurated, moderately adherent, and fixed. The left lobe was much more prominent and much more indurated and larger than the right, extending well downward toward the perineum and pelvic wall. Outer edge was quite sharp and hard. The right seminal vesicle was about the size of the finger, smooth, very hard, and fixed; induration extended upward and outward in the vesicles which became gradually smaller as far as the finger could reach. The left seminal vesicle was much larger than the right, irregular, nodular, extremely fixed, very hard induration extending outward, and adherent far back, almost to the sacrosciatic notch. No glands were felt in the sacral fossa on either side. The membranous urethra was extremely hard, evidently involved down to the triangular ligament. The bulb of the urethra was not much enlarged, but definitely indurated and apparently involved. The rectum was smooth; the muscularis adherent but the mucosa soft and adherent. X-ray of pelvic bones did not show any demonstrable lesions. In three months 3200 milligram hours of radium were given, 2500 milligram hours per rectum and 700 milligram hours per urethram. At the end of this treatment rectal examination showed the rectum to be a little thickened but not ulcerated. The prostate was about normal size, fairly smooth, and a little firmer than normal. On pressure it seemed distinctly atrophic and thinner than usual. The indurated right seminal vesicle had improved immensely, was still a little firmer than normal and distinctly adherent along the outer edge, but one would not recognize it as being malignant. The left seminal vesicle was drawn outward, slightly indurated, considerably adherent, and possibly one or two small glands were felt far out, but this vesicle would not be recognized at all as malignant. The membranous urethra was a little broader than normal and somewhat indurated and fixed.

Patient's symptoms have improved and remained permanent for the past 4½ years. He voids freely every 3 hours during the day and gets up once at night. He has gained weight and is enjoying the natural mode of life. Recent report by his family physician states that there has been no change in the prostatic tissues for the past 4 years.

This splendid result was obtained with 3200 milligram hours in one series.

No. 5446, 80 years old, was admitted October 12, 1916 complaining of frequent and difficult urination. The urinary symptoms had been present for 2 years. Size and force of stream had become greatly diminished, although he had never had complete retention. At times great urgency and difficulty in starting the stream were present but he had never had haematuria.

Rectal examination showed a prostate which was a little more prominent than normal, slightly enlarged, a little irregular, indurated, and almost of stony

hardness. Prostate was moderately fixed; median furrow and notch absent. Both lobes were about equal in size. The right seminal vesicle was corded, moderately indurated and adherent, but no enlarged glands were felt on this side. The left seminal vesicle was about an inch broad, flat, considerably indurated and adherent, and the intervesicular space was partly filled with infiltration. The membranous urethra was obscured by adhesions and low position of the prostate. The rectum was smooth, movable and apparently not invaded.

Cystoscopic examination showed residual urine of 325 cubic centimeters. The bladder was quite irritable and would hold only 200 cubic centimeters. There was no cleft anteriorly and the right lobe was very slightly enlarged. The median lobe was considerably enlarged as a sessile enlargement. The left lateral lobe was not intravesically enlarged. The mucous membrane was everywhere smooth. The bladder was considerably trabeculated. The ureters were readily seen on hypertrophied ridges with pouches in front and behind them.

During the next 2 months the patient received 2000 milligram hours of radium, 500 milligram hours given per urethram and 1500 milligram hours per rectum. Patient then complained of only slight irritation in the rectum. Rectal examination showed prostate not to be enlarged. The median furrow was very narrow and shallow, being almost obliterated. The right lobe was more prominent and apparently extended beyond the mid-line; the surface

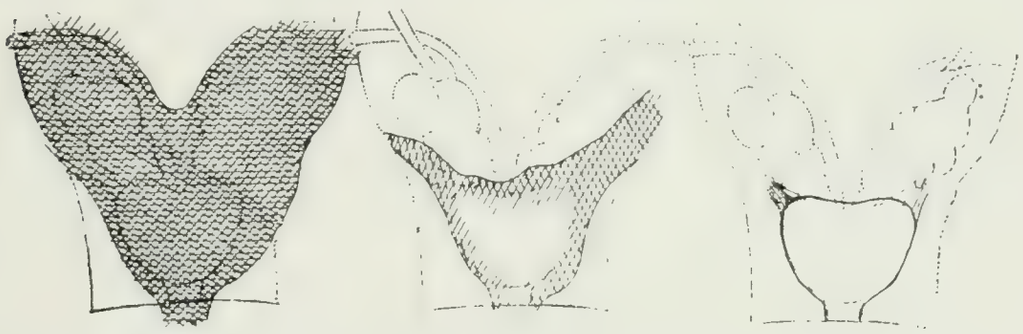

Fig. 1.—Case 12.—Chart showing involvement on admission, April 27, 1921; after treatment consisting of 1500 milligram hours, May 24, 1921; and after 4400 milligram hours, June 21, 1921.

was smooth and its consistency, although somewhat firmer than normal, was not of stony hardness. "It would, however, even at the present time be regarded with suspicion." The lobe was quite fixed. The left lobe was similar to the right, somewhat less indurated. In the region of the right seminal vesicle the induration described in the right lobe was felt and the vesicle was corded but appeared freely movable. A definite intervsicular plateau could be felt, the upper margin of which appeared to be quite thickened and of the consistency of gristle. The left vesicle except for a slight induration presented nothing of note. The mucous membrane was freely movable except for a slight thickening in the region of the right vesicle. The right seminal vesicle appeared normal. Patient's urinary symptoms were greatly improved. He voided every 2 to 3 hours. Residual urine was only 30 cubic centimeters.

Six months after the beginning of radium treatment he could hold his urine for 5 or 6 hours. Rectal examination showed still less induration and residual urine dropped to 10 cubic centimeters. There was no pain, hesitancy, or difficulty in the act of urination. (No treatment was given at this time. This was a grievous mistake). Two months later rectal examination did not show any evidence of carcinoma and the picture was one of a slight grade of prostatitis and seminal vesiculitis. Fourteen months after admission the rectal examination remained the same as at 8 months, but the residual urine had increased to 75 cubic centimeters. Patient then apparently remained perfectly well for 3½ years when he began to have urinary difficulty and complete obstruction soon followed. Rectal examination at this time showed prostatic hypertrophy of slight degree. It was everywhere soft and elastic. The right seminal vesicle was not enlarged nor hard. The left was somewhat adherent but compressible. There was moderate oedema of the rectal mucosa. There was nothing to indicate recurrence of the cancer. Cystoscopic examination,

however, showed a necrotic mass on the left side of the bladder which involved a portion of the vesicle orifice. Whether this was an ulcer due to radium given 4 years previously or whether it was cancer was not determined. X-ray did not show any involvement of the bony pelvis.

Since the patient had obstruction to urination which was due to contracture of the neck of the bladder and to the infiltration of possible cancer growth, it was decided to give him more radium. Sixteen hundred milligram hours were given per rectum, 500 milligram hours per urethram, and 400 milligram hours intervesically. In one month patient began to void every 3 to 4 hours and residual urine ranged from 10 to 110 cubic centimeters. He had very little rectal irritation. He would leave the ward to go to an afternoon matinee and return without any urinary discomfort. Last rectal examination showed no enlargement of the prostate. The seminal vesicles were soft and elastic. There was no evidence of carcinoma. Cystoscopic examination showed ulceration of left side of bladder. Prostatic orifice showed considerable oedema. Left lateral margin was negative. Just behind it was a small necrotic mass. With finger in rectum and cystoscope in urethra, trigone did not seem to be thickened, as it is in cases which have definite carcinoma of the prostate. There was no infiltration of the suburethral tissues. Died, at home, of pneumonia 1 month later. Necropsy not permitted.

No. 5759, 75 years of age, was admitted in March, 1917. The history dates over a period of 2 years. Nycturia was the first symptom. Frequency of

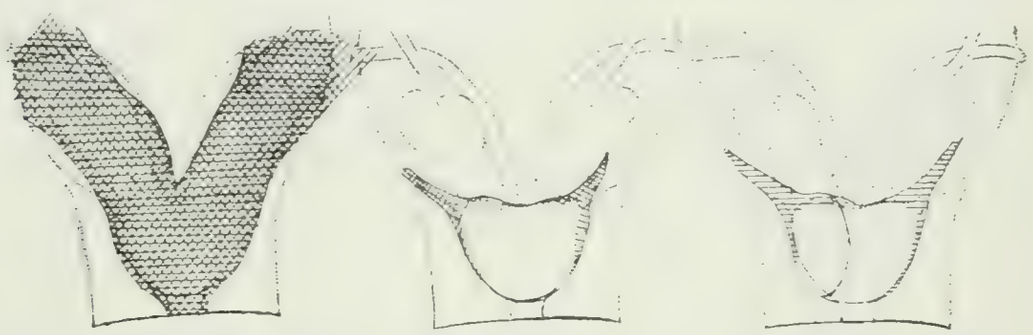

Fig. 2.—Case 15.—Chart showing involvement on admission, April 21, 1921; after 2700 milligram hours, June 6, 1921; and after 4200 milligram hours, June 15, 1921.

urination gradually increased both night and day so that he had to void every hour. Size and force of the stream had diminished so that there was considerable dribbling. He had never noticed any haematuria.

Rectal examination showed that the prostate was quite irregular on the surface. In the left lobe toward the periphery there was a sharp edge, rather far in the mid-line between the seminal vsicles almost as far as the finger could reach. The seminal vesicle did not seem to be particularly indurated. The membranous urethra was soft, as was also the apex of the prostate. The growth seemed to lie between the seminal vesicles involving the posterior portion of the prostate.

Cystoscopy. The instrument was readily introduced and found 50 cubic centimeters residual urine. The bladder showed evidence of obstruction. The walls were trabeculated and there were a number of cellules. The prostatic orifice showed no clefts, some irregularity, and some oedema, but no intravesical lobes. The trigone was visible. With finger in rectum and cystoscope in urethra it was possible to make out marked thickening in the base of the prostate as the shape of the instrument could not be felt. There was present a marked indurated mass between the instrument and the finger.

The patient received three series of radium treatments during the next 6 months. The first series was given from March 16 to April 4—700 milligram hours per rectum and 200 milligram hours per urethram. On April 6 patient was voiding every 5 or 6 hours during the day and getting up once at night. He was also passing small amount of mucus per rectum. Rectal examination showed both lobes of the prostate less resistant than at first examination. Along the border of the right lobe near the base was still quite marked induration. This was true also of the left side.

On May 23 patient returned for second series of treatments. Rectal examination showed prostate considerably larger than normal, somewhat irregular, definitely softer than before the radium treatment. The left lobe was only slightly larger than normal. There was a hard area in the periphery of the right lobe and some induration at the base of the right seminal vesicle. There was no thickening of the rectum. The patient then received 600 milligram hours of radium, 500 milligram hours of which were given per rectum and 100 per urethram.

Patient received third series of radium treatments in September of that year at which time he was given 10 hours of radium of 100 milligrams each,—800 per rectum and 200 per urethram. Patient showed moderate rectal irritation, which lasted for 4 weeks only. Urinations remained normal. Rectal examination in November showed very little change in the rectal mucosa and no ulceration. The prostate was a little larger than normal, irregular, compressible, and adherent.

Two years later the patient was again examined. Symptomatically he had been free from frequency and pain. Residual urine was 15 cubic centimeters. There was a slight stricture of the urethra which was easily dilated. Rectal examination showed the prostate broader than normal and the vesicles broad and adherent; but neither the prostate nor the vesicles were very markedly adherent. The surface was fairly smooth and flat. It would have been impossible to make a diagnosis of carcinoma at this time.

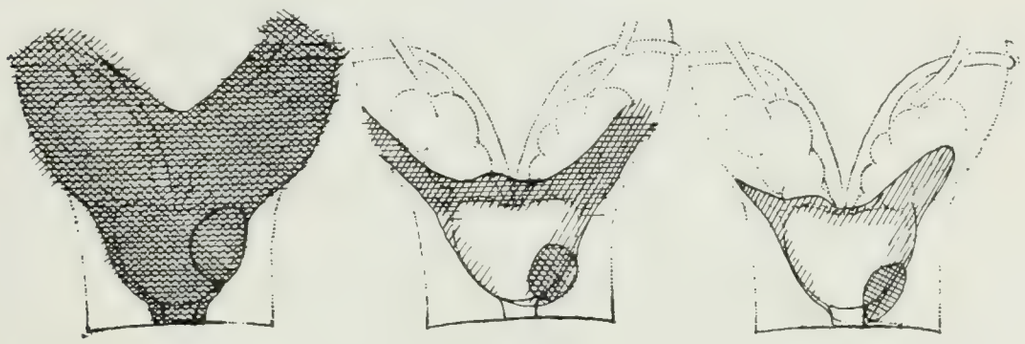

Fig. 3.—Case 18.—Chart showing involvement May 10, 1921; after 3200 milligram hours' treatment, June 7, 1921; and after 4700 milligram hours, June 22, 1921.

Patient returned in July, 1920, stating that he had been in excellent health but during the past 6 weeks had noticed a little frequency of urination. At times he would void every 10 minutes, but could hold urine for 5 or 6 hours. He slept well and was doing his usual work. Prostate was a little broader than normal, moderately indurated, and slightly adherent. Above the prostate was a plateau which extended across the pelvic cavity, more prominent on the left side. In the mid-line there was a small area simulating an excoriated area. The patient was given 1100 milligram hours of radium per rectum over the seminal vesicla regions with the result that there was resorption of the indurated areas.

Patient has not been examined for 1 year but he recently reports that his general health is excellent, he has maintained his weight, and is doing ihs usual work. He is voiding every 6 hours without difficulty. There is no pain in the back of thighs. He writes: "I have no symptoms that can be referred directly to the prostate and bladder."

This is a case which apparently could not endure the concentrated form of treatment. The patient received 3100 milligram hours in four series. The result has thus far been most encouraging.

Twenty-Three Cases With No Relief of Symptoms

In contrast with symptomatic, local and good results, a certain number of cases failed to respond to radium treatment. Many of these received small doses, too small to produce any definite action on the carcinoma, while others received 1200 to 1400 milligram hours and should

have shown at least a change in symptomatic condition. Such was not the case. None of these cases showed any ill effect from the radium, and there was no reason why treatment should not have been continued as far as the charts indicate, except that in a few instances patients left the hospital of their own accord. Twenty-three cases did not react to radium. A further study of these cases showed that the average amount of radium given was only 625 milligram hours, while the average for

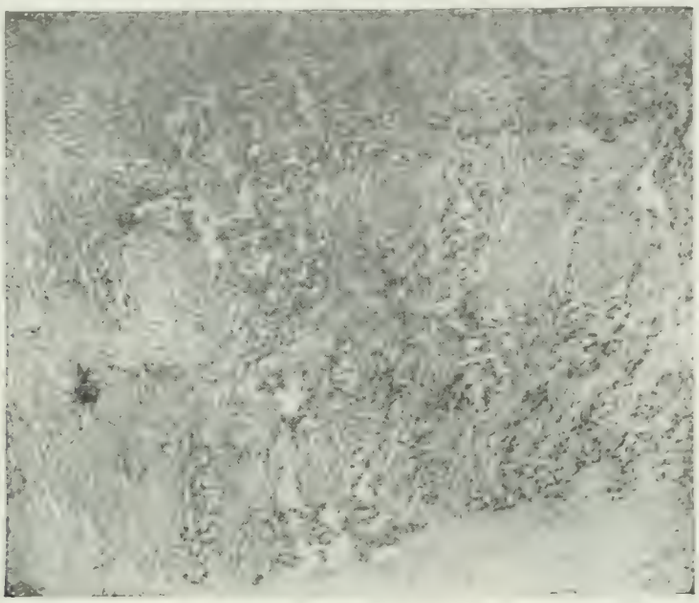

Fig. 4.—Scirrhus cancer of the prostate.

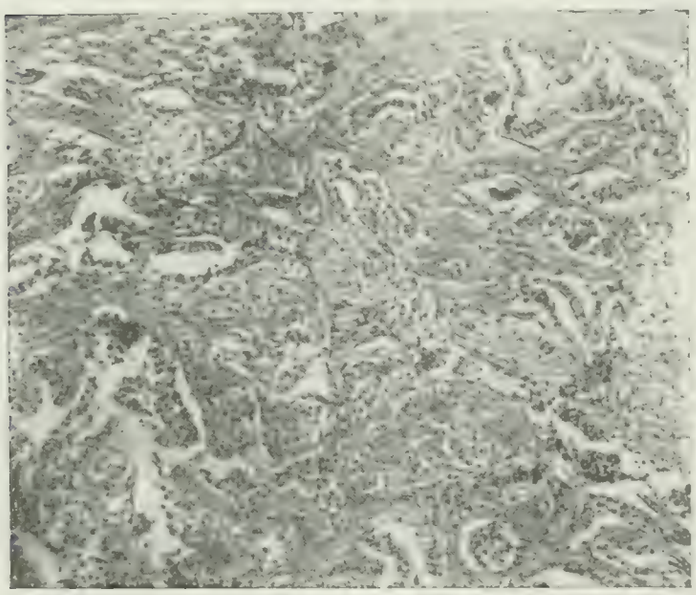

Fig. 5.—Adenocarcinoma of the prostate.

those receiving at least some improvement was 1415 milligram hours.

There was only one case which showed local results without symptomatic. This case proved to be one with well-developed growth along the urethra. He had received 1400 milligram hours of radium, all given per rectum. Had he been given extensive treatment to the urethra and internal vesicle orifice, symptomatic results would almost undoubtedly have been obtained. In no case did we find that radium stimulated the growth of the cancer. It is, therefore, quite clear that those who did not

show any relief of symptoms did not receive radium enough, while the next grade obtained a symptomatic improvement, and when still more radium was given, local results were obtained.

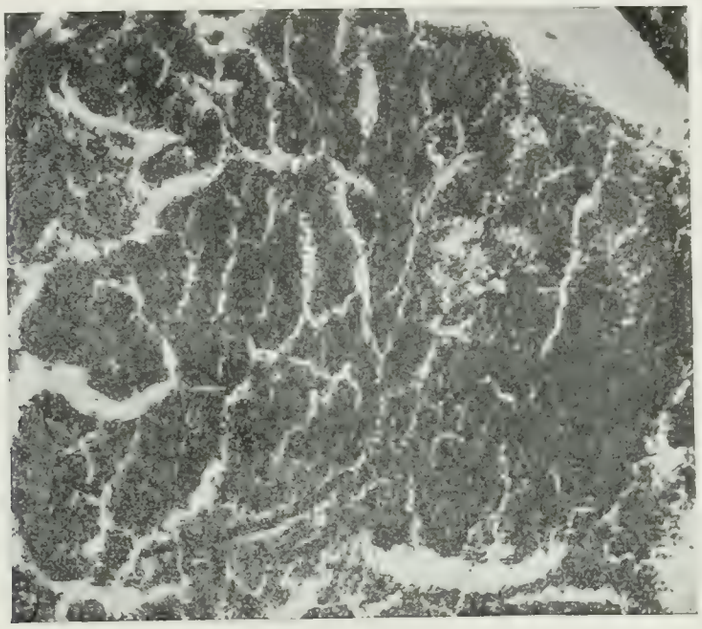

Fig. 6.—Cellular or medullary cancer of the prostate.

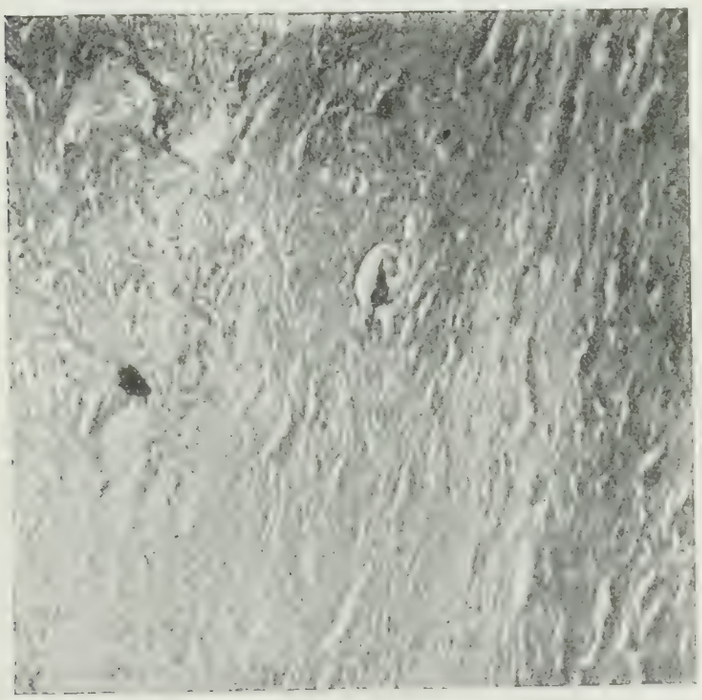

Fig. 7.—Adenocarcinoma showing complete destruction of the cancer with marked fibrosis following radium treatment.

Irritation From Radium

The irritation from radium rays has been one factor for consideration in this therapy. It was not until after this analysis had been completed that we were able to combat the main objection to radium treatment. Twenty-eight cases showed more or less local discomfort. Some were very slight, while others were severe. However, all are included in this series so as to definitely determine the factors involved. There

were no general systemic reactions such as nausea, vomiting, chills, fever, etc. All symptoms of irritation were localized and manifested by rectal and urethral burning, urgency for stool, passage of mucus, and occasionally blood per rectum, and in two cases ulceration of the rectal mucosa.

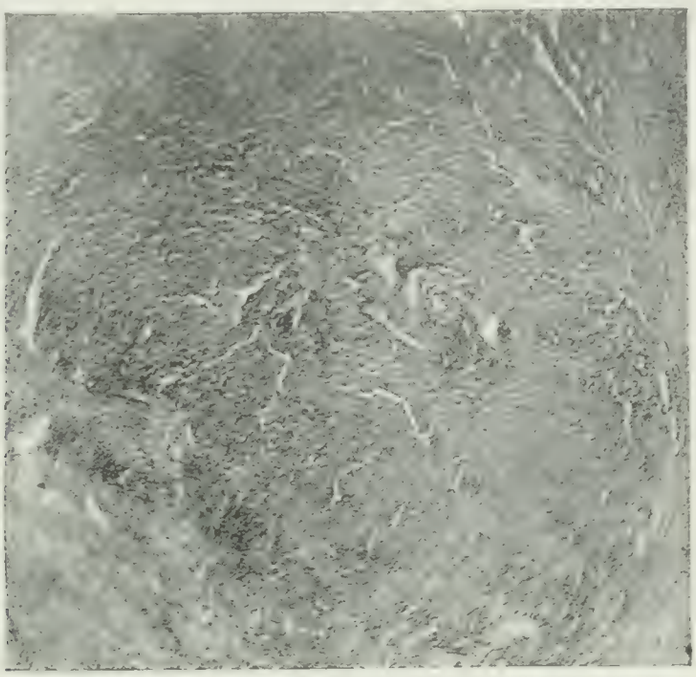

Fig. 8.—Adenocarcinoma showing necrosis due to radium applied intraglandularly.

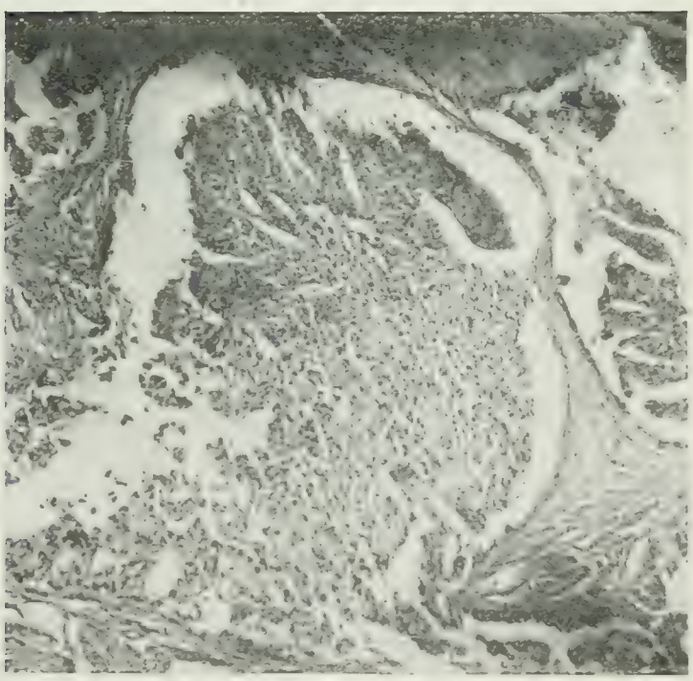

Fig. 9.—Adenocarcinoma showing variable effect of radium. One-half of the alveolus shows degenerative changes while the other half shows healthy cancer tissue.—3 weeks after termination of radium series.

Rectal. Irritation of the rectum in the form of an aching, smarting, and burning sensation was noted in all of the 28 cases. In 9 cases it was very slight and hardly worth mentioning; it lasted for a few days and

caused no change in the patient's daily routine of affairs. In other cases the irritation became intolerable. Especially was this noted on evacuation of the bowels or when fæcal matter reached the rectal area treated. The patient would then ask for an enema or opium suppository, or both. The rectal irritation began at about the tenth treatment and often lasted for 2 or 3 weeks after the series had ended. The more severe cases would complain of some pain as long as 6 months afterward.

Mucus. The passage of mucus per rectum was noted in 19 of the 28 cases. Mucus did not appear until several days after the patient complained of burning and smarting, or during the latter part of the series. Usually it was an indication to dispense with the treatment. Some cases were treated until they could not tolerate the applicator in the rectum. Those cases receiving large doses at one sitting or frequent treatments in the same area were first to show evidence of irritation. In some of the severer cases frequent bowel movements accompanied with mucus or evacuations of mucus alone were demonstrable. Never were there over eight to ten movements in 24 hours in the most severe cases, but there was moderate tenesmus and straining at stool. In none of the cases was it permanent; in most cases it subsided after 3 weeks, but in two cases it persisted for 8 months. Urgency for stool was present in 6 of the cases discharging mucus. Blood-streaked mucus was noted in 4 cases only.

Urethral. Smarting and burning sensations were the main complaints in this region, although complete retention occurred in 3 of the cases, 2 to 5 days following the first treatments. After 2 or 3 days of complete retention they began to void and in about one week the size and force of the stream gradually returned to much better quality. Five of the cases complained of urethral irritation. These symptoms were never so prominent as the rectal distress nor were they as prolonged.

Ulceration. Only two cases developed ulceration of the rectal mucosa. One healed entirely in 10 months and the other developed a rectourethral fistula 4 months after the treatment (recently 2 other cases of rectal ulceration have appeared). The latter case showed on admission a hard nodule in the center of the prostate with little involvement of the lower portions of the seminal vesicles. He received 2800 milligram hours of radium, 200 of which were given in the rectum over or near the nodule. The result was complete resorption of the mass and the development of ulceration. The patient complained of considerable burning and tenesmus for 6 months. He, however, suffered very little from the small fistula. He makes a statement 6 years afterward that he is doing as much work as ever and feels perfectly well, except that he has in 24 hours three to four bowel movements, a good part of which is composed of urine. No fæcal material has ever passed the urethra. His urinations are not oftener than normal and he does not have to get up at night. He is apparently cured of the cancer, although he had never returned for further examination. These two cases occurred early in the use of radium. None of the last 150 cases have developed ulcerations. It is certain that they can be avoided and must be kept in mind when giving a large series of rectal treatments. Large urethral treatments will give rectal irritation as well as rectal treatments, and occasionally rectal treatments may cause a diminution in the size and force of the stream with exaggerated hesitancy, but this lasts only for a few days at most. If 150 to 200 milligram hours are given at one sitting in one place there is considerable smarting and burning in that area in 4

days which lasts for 3 weeks. Generally it may be stated that treatments exceeding 150 milligram hours in one place at one sitting or the same area treated oftener than once a week to 10 days will produce an irritation.

With the intensive treatment now used, no ulcerations have developed and the patient is able to tolerate 4000 milligram hours better than 2000 milligram hours given by the former method (2 recent cases may require us to modify this statement, H. H. Y.) Frequently a patient passes mucus and has from two to four stools a day with some discomfort or tenesmus, but these symptoms finally disappear. None have complained of constipation. Needles introduced directly into the cancer through the perineum for a 500-milligram-hour treatment have not caused any irritation or discomfort of any sort.

There have been no general systemic reactions with malaise, nausea, vomiting, or elevation of temperature. As a rule, the patients feel better and are able to tolerate a larger number of treatments if they are allowed the freedom of out-of-doors, and are treated as ambulatory patients rather than if we house them in their rooms for 4 or 5 weeks. Hygienics play an important role in the treatment of malignant disease as well as in other diseases and should be kept in mind in the treatment of cancer of the prostate with radium.

Mortality. The expectancy of life of a patient with cancer of the prostate is a variable factor. As a rule, prostatic cancer is a slowly developing malignancy. In estimating the length of life of a patient from the beginning of the symptoms it is almost impossible to be accurate, for many have an extensive invasion of cancer before any urinary symptoms appear. It seems, however, to be the only method which we have at our present command. The average length of life after beginning of symptoms for the 48 cases known to be dead is 2.54 years. Twenty-two patients were not heard from. They failed to answer the second questionnaire, and a third sent to the family physician failed to elicit further details regarding them. The statistics show 13 cases who are not improving and have now lived an average of 3.6 years since onset of symptoms. Many of these have improved symptomatically, and locally there has been a softening of the prostatic tissues, but there is a general decline in health due to metastases. There are 12 patients still under tratment who are showing improvement. The average length of life in this group is 4.4 years.

Those cases which are considered as good results have now lived an average of 6 years since onset of symptoms. There are 5 cases in this group. Table XI shows that, even where cure is impossible, treatment with radium tends to prolong life and that in a certain number of cases a cure may be expected.

We have no definite histological proof that radium is a cure for inoperable cancer of the prostate, but we may draw valuable conclusions regarding its effect and in this way guide our methods of application of the gamma rays in such a way that in the future it may yield a much higher percentage of good results. There is no doubt that radium is as good a therapy as any that we have at our command; that patients may be relieved of much pain and discomfort in their last years, even if a cure cannot be instituted in a majority of the cases. Relief of symptoms is what the patient comes to us for just as he does in any other disease, and why should we not give him relief or even the benefit of medical science, if a cure cannot be obtained? Because a case is incurable is no

reason why our profession should turn him over to the land of opiates. He should at least be given the benefit of radium therapy even if only symptomatic results can be obtained.

Table XII shows the result in 18 cases receiving at the first series the more concentrated form of treatment. The results obtained are too recent to pronounce cures and sufficient time has not yet elapsed to allow the radium to produce its total effects symptomatically and locally; but all cases exept one show on discharge a very remarkable change in both consistency and size of the carcinoma. The detailed rectal findings together with the prostatic charts of three of the cases are given. These are not exceptional cases, but are cases in which, when there are no bone metastases, the results are more uniform than heretofore obtained.

Case 12 (Table XII). April 27, 1921, rectal examination shows few external haemorrhoids, with anal sphincter of good tone. Prostate is markedly enlarged and projects into the rectum. Median furrow and notch are just made out. The right lobe is markedly indurated, slightly irregular and markedly adherent externally. Left lobe is also markedly indurated and adherent externally, but is not so markedly indurated as the right lobe. Induration in both lobes, especially on the right, is of stony hardness. The process on the right side extends up into the vesicle, which can be felt markedly indurated. Few enlarged glands on the inner surface. The process on the left side extends up to a certain extent to the seminal vesicle, which is also greatly indurated.

May 7, 1921, patient has been treated here with radium by rectum and urethra, receiving 15 treatments, one hour each, with 100 milligrams of radium. He stood this treatment well. Until this morning we had very little difficulty in urinating but micturition was very difficult this morning. Patient got up 3 or 4 times last night, being able to void only small amounts. He was catheterized this morning and 750 cubic centimeters residual urine found. He is going home for 2 weeks and is instructed to be catheterized 2 or 3 times daily, if necessary.

May 24, 1921, rectal examination shows prostate enlarged moderately, the right being much larger than the left. The left lobe is only slightly larger than normal, smooth, slightly indurated, elastic, only slightly adherent. The upper end is slightly indurated, the induration extending upward and outward along the outer side of the left seminal vesicle, which is now soft. This induration is only of slight degree. The right lobe of the prostate is moderately enlarged, slightly irregular, slightly indurated, considerably adherent along the outer edge and near the apex, at which point it is much more indurated than elsewhere and very adherent. (Seems evident that not enough treatment has been given at this point). At the upper end of the prostate there is a line of irregular infiltration, of considerable degree, which extends upward and outward along the pelvis, as far as the finger can reach. Slightly enlarged glands are palpable here. The seminal vesicles are distinctly palpable, probably invaded. Between the vesicles there is slight induration. (See Fig. 1). The membranous urethra is broader than normal, moderately indurated. Patient then received 2900 milligram hours.

June 21, 1921, patient returns for observation for the third time. He has had no treatment for 2 weeks. Patient stated that he has had a good deal of discharge from "bowels," at times is constipated, and at other times has marked frequency of stools if he takes a purgative. There is no pain or discomfort in the rectum, except during stool. He passes a good deal of mucus, but this condition is improving. Vesical condition is very greatly improved. He voids urine at normal intervals, without difficulty or pain. There is no pain in back, hip, or thighs. General condition has been fairly good. He simply returns for observation.

The anal sphincter is in good condition. Prostate is now a little broader than normal especially on the right side. Left lobe is about normal size and consistence and is not adherent. Left seminal vesicles are apparently not indurated and only slightly adherent along the outer edge. The right lobe is little broader than normal, slightly indurated and slightly adherent. There are a few adhesions running up along the wall on each side. The condition does not even now suggest carcinoma. Between the vesicles the tissues are quite soft. Examination causes slight bleeding from the rectum.

Case 15 (Table XII). April 21, 1921, rectal examination shows sphincter of good tone, with no external haemorrhoids. The prostate is moderately enlarged, projects into the rectum, median furrow and notch obscured. The right lateral lobe is smooth, elastic moderately indurated. The left lobe is more prominent than the right, smooth, elastic, moderately indurated and somewhat adherent. The seminal vesicles are drawn out and adherent laterally with some induration at their bases. There is no intervesicular plateau of induration. The base of the bladder feels soft. On the left side a small hard body is felt, probably a phlebolith.

Cystoscopy. Prostatic orifice shows no cleft anteriorly. There is a markedly elevated median portion. With finger in rectum and cystoscope in urethra, the trigone is not thickened. Median portion of prostate is much thicker and longer than normal and quite firm, somewhat nodular. The left lateral lobe is nodular and indurated but still somewhat compressible, the right lateral lobe the same. The whole prostate forms a transverse mass around the shaft of the instrument and the induration and enlargement beneath the urethra extends to the apex, in other words there is a suburethral thickening which extends practically to the apex of the prostate and which itself suggests malignancy. Induration, however, is not of stony hardness.

June 6, 1921. Patient has now had 18 treatments per rectum, 4 per urethram, and 5 by bladder, a total of 27 treatments. During the past month his general condition has improved remarkably, he has gained 5½ pounds in weight, appetite has improved, and patient feels very much stronger. Patient voids about every 3 hours, moderate-sized stream with natural act of micturition, force of stream not quite normal. No headache, backache, or pain in the thighs. Patient has had some rectal irritation, passes a small amount of mucus but never any blood. Patient has had some frequency of bowel movement, about 7 or 8 a day, but the rectal condition has now improved so that the bowels move only once or twice a day. Patient considers himself remarkably improved.

Rectal examination, June 15, shows a prostate that is now normal in size and consistence, not nodular, not indurated except slightly, not adherent. The change is really remarkable. Right seminal vesicle now feels only slightly indurated along the outer edge, no enlarged glands or adhesions are left. Left seminal vesicle is also small and soft, not indurated or adherent. Rectal wall is somewhat swollen and redundant but does not feel ulcerated.

From examination at present one would never suspect that this patient had carcinoma of the prostate and seminal vesicles.

Case 181 (Table XII). May 10, 1921. Rectal examination shows anal sphincter good, somewhat spasmatic. Prostate is very irregular. Left lateral lobe is somewhat nodular, extremely indurated, fixed, induration almost of stony hardness and extending down along the membranous urethra but not palpable in the bulb, external to the triangular ligament. Right lobe of the prostate is also irregular, markedly indurated, extremely prominent as you go backward and the induration extends forward to the left lateral wall of the pelvis and obscures the seminal vesicles. This indurated mass makes it impossible to feel that the left seminal vesicle. At the upper end, on both sides, there is a transverse plateau of marked irregular induration, which extends from one side of the pelvic wall to the other, upward, as far as the finger can reach and beyond. Rectum also is everywhere smooth, and on the left side it is freely movable upon the prostate and seminal vesicle. On the right side the musculature is invaded and rectum is fixed.

June 8, 1921. Patient has had about 32 treatments. He complains only when he goes to stool, desire for which is very frequent. He is not required to get up at night for stool. He has not passed any blood but has passed a good deal of mucus. Gets up once or twice at night to void, voiding freely, good stream, without much pain. Patient has had only four treatments per urethram and none with needles through the perineum. Treatment over the seminal vesicles and along the pelvic wall are also apparently incomplete.

Rectal examination, June 22, shows anal sphincter in good condition. Rectal wall is everywhere smooth, it is not particularly tender and no areas of ulceration or excoriation are felt. Left lobe of the prostate is now about normal in size, only slightly indurated. Little nodule present at the upper end, where the induration runs upward and outward along the lateral wall

of the pelvis, as far as the finger can reach. The induration in this region is only moderate in degree, likewise between the two vesicles as shown in diagram. The point in which there has been less treatment is on the right side along the outer edge and at the apex.

The cure of cancer of the prostate and seminal vesicles has thus far been a difficult problem. Surgery has failed except in a very few selected cases where the cancer is small and limited to the prostatic tissue. We attribute the failure to (1) the inaccessibility of the tumor, (2) the late appearance of the case in the clinic, (3) cases with bony metastases, (4) improper technique and (5) insufficient radiation. These difficulties are rare in surface cancer. Since the action of radium varies inversely to the square of the distance, it is, therefore, necessary to apply the gamma rays as near as possible to the tumor to obtain the maximum effect. With this basic principle in mind and avoiding the severer irritations, we should be able to control cancer of the prostate in those cases which have not developed metastases beyond the seminal vesicles. Large doses of radium in the shortest possible time applied to all surfaces of the prostate, viz., per rectum, per urethram, and per vesicam, apparently control the peripheral growth. Cases which have shown recurrence have done so in the mid-prostatic and vesical orifice and seminal vesical areas. More careful technique has controlled all the areas except the mid-prostatic portion.

Intraglandular radiation with needles adds much to supplement the surface treatments. Either treatment without the other is inadequate. If needles alone be used then the tips of the seminal vesicles escape radiation. Cass should be examined every 3 months to detect any area of recurrence so that further radiation may not be delayed. If rigid technique with massive doses be used, we believe that cure of cancer of the prostate, provided there are no metastases beyond the seminal vesicles, lies within the scope of radium treatment.

Conclusions

1. Radium gave symptomatic relief and return of normal urination in 75 per cent. of the cases.

2. Radium relieved the pain in the back in 50 per cent. of cases suffering from metastases.

3. Irritation from radium can be avoided by treating widely remote areas in successive treatments and by alterating between rectal, urethral, and vesical applications.

4. At least 1000 milligram hours must be given to produce any symptomatic improvement.

5. Fourteen hundred milligram hours must be given to produce any perceptible change in the tumor mass.

6. Three thousand milligram hours must be given to produce symptomatic and local results in the same patient.

7. Four thousand and 5000 milligram hours in a period of 6 to 8 weeks should be given if possible, in addition to needle treatments of 500 to 2000 milligram hours through the perineum.

8. Cases which did not respond to radium did not receive sufficient radiation.

9. Large doses must be given in as short a period as possible to produce maximum results.

10. No general systemic reactions have been encountered.

11. Combined extraglandular and intraglandular radiations apparently give the most satisfactory results.

12. Thus far we have no actual proof that radium has produced an actual cure for cancer of the prostate and seminal vesicles, although three cases remained free from symptoms and tumor growth for more than 4 years and many others show on rectal examination a condition of the prostate which does not now resemble cancer.

II. Results of Radium and Operation in Cancer of the Prostate (33 Cases)

Radium and surgical methods have been used to give relief in some of the more difficult cases of cancer of the prostate and seminal vesicles. Herein lies a possibility which must not be overlooked as better results may be obtained in a certain number of cases by a combination of radium and surgery. Questions naturally arise: Can we remove the cancerous tissue after it has been treated with radium and increase the opportunities for cure? Can we remove most of the malignancy and treat the remainder with radium? Do we spread the cancer by operative measures? Can we obtain better results by preoperative and postoperative application of the radium, or can we at the time of operation remove as much of the cancer as possible and then apply massive dose treatments?

The operative series is a small one consisting of 33 cases. Practically all the possibilities previously mentioned have been carried out. It is certain that operative measures do not add to the risk of metastatic development. A series of 100 cases which were operated on without radium treatment lived almost as long as cases which were not operated on and which received radium treatment alone but there was no attempt to cure these cases.

This series of cases is similar to the series of 100 cases previously treated with radium alone. Ages range from 58 to 80, the largest number of cases being found in the seventh decade. There were three cases under the sixtieth year, twelve between 60 and 70 and six between 70 and 80. The prostate was generally invaded in all the cases. Both seminal vesicles were involved in all except three and these showed an extensive infiltration in one vesicle. The average number of milligram hours given before operation was 1380, ranging from 400 to 4000. Treatments extended over a period of 1 week to 14 months. The symptomatic and functional improvements were not marked, being only 26 per cent. None of the patients were entirely relieved from all their symptoms. Thirty-eight and eight-tenths per cent. showed local improvement, but not complete resorption of the cancer.

The operations performed were of two types: (1) conservative perineal prostatectomy—by means of which the cancerous tissue about the prostatic urethra and vesical orifice was removed: (2) subtotal prostatectomy—by means of which the capsule of the prostate was removed together with the cancer. There were two operative series: one which received pre-operative radium treatment and another which received postoperative radium treatment.

There were 28 cases which received radium before operation. These were treated per urethram and per rectum: 7 cases received rectal treatments alone and 20 received rectal and urethral treatments. The total radiation varied from 400 to 4000 milligram hours, the average radiation

being 1600 milligram hours. Most of the cases were operated on at the end of the series of radium treatment by the conservative method. Nine cases received massive doses of radium at the time of operation. A 100 milligram capsule was inserted at the time of operation into the wound and allowed to remain from 5 to 8 hours. No untoward results have occurred and there has been no interference with the closure of the wound, in fact they have healed as rapidly as the benign hypertrophy cases. No fistulæ have developed.

Postoperative radium treatment. Five cases were operated on first and then given radium. Two received 1600 milligram hours at time of operation; the other three were given 100 milligram hours' treatment after the wound had healed. These cases, like the others, left the hospital voiding normally.

Results. The time elapsed since treatment has not exceeded 4 years, so it is quite possible that some may develop a recurrence. Four cases have now lived 3 years and are apparently entirely relieved of symptoms and local tumor. Statistics show that 12.1 per cent. of the cases have an excellent result—classified as "good result;" 66.6 per cent. were improved; and 21.2 per cent. remained unimproved. The cases showing good results have a complete subsidence of all urinary symptoms and no furthr development of local tumor. Those cases improved show relief of symptoms but rectal examination discloses active cancer present. The 21.2 per cent. unimproved did not get relief by operative measures. There was still urinary difficulty with palpable cancer in prostatic tissue. Of the 33 cases 51.5 per cent. have died. Death was due to metastases in all cases. These cases lived from 5 to 22 months—an average of 11 months after operation. Those cases in which good results were obtained received a combination of radium before and after operation. The amount of radium before operation did not exceed 2000 milligram hours in 2 of the cases. Two received 2500 and 3100 milligram hours. The operations were the conservative type. The amount of radium given after operation ranged from 1200 to 2100 milligram hours, giving a total radiation of 3000 to 4000 milligram hours. These cases have not been examined for 1 year, but they report that their urinations are normal. Last rectal examination, 2 years after operation, did not show any return of cancer.

There are two cases recently treated with large pre-operative doses of radium. Each received 4000 milligram hours. Two weeks later a perineal prostatectomy was done. Both specimens removed at operation showed hypertrophied tissue invaded by cancer. The capsule stripped readily and was free from cancer. Apparently complete resorption of the cancer had taken place in the capsule. It is fair to believe that control of the growth has been accomplished in these cases and that by removing the adenoma a cure has been obtained. Those cases receiving only postoperative radium apparently did not receive sufficient radiation as they occur in the improved group.

Histological Picture

Study of the specimens removed at operation is the only method of deducing accurate conclusions regarding the effect of radium. The histological picture is by no means uniform. The sections from some of the specimens removed after application of 800 milligram hours of radium show considerable change in the periphery, while others taken from specimens which had received 2000 milligram hours failed to show

any effect of radium whatsoever. None of the specimens showed complete destruction of all the cancer tissue, although there were areas in which destruction was complete. Just why there was such irregularity in the histological findings we do not know, but there are several possibilities which must be considered, viz., kind of cancer, the frequency and method of treatment, and the specific or selective action of radium for certain cells.

The action of radium has been found to be of two kinds: (1) a gradual disappearance of the cancer tissue and the development of fibrous tissue and (2) necrosis.

The gradual changes produced by radium have been well described by Drs. Young and Frontz (2) and Dr. Alter (3). The effect of radium does not correspond in all cases to the amount of radium given. Some tissues show marked changes while others show little change that can be ascribed to radium. The periphery of the specimens naturally shows the first evidence of radiation. Different conditions of degeneration can be easily seen in many of the specimens, such as pyknosis of the nuclei, vacuolization, shrinking of the cytoplasm, and in some cells a few poorly stained granules. Other cells show granules taking very deep stain. Increase in fibrous tissue is a prominent factor in most of the sections. It is firm, the strands are packed tightly together and form a dense, hard tissue. Between some of the layers of fibrous tissue small darkly stained granules or outlines of a few cancer cells may be seen, indicating complete destruction of the cancer with development of fibrous tissue.

In all the cases treated with extraglandular methods no necrosis of tissue was found. Whenever a change occurred it was a picture of gradual melting away of the cancer tissue and a development of fibrous tissue. One specimen had been treated intraglandularly with two needles. Each needle contained 12.5 milligrams of radium and was allowed to remain in position for 24 hours. The operation occurred 2 weeks later. Sections from this specimen showed necrosis of all the tissue within a radius of 4 millimeters. The connective tissue stroma as well as the cancer forms a necrotic area (see figure 5). No such areas have been seen in the other specimens although some received 4000 milligram hours.

We have considered the fact that different kinds of cancer might react differently to radium and cause a diversified histological picture. There are three kinds of cancer of the prostate thus far recognized: (1) the scirrhus with small cell nests and large amount of fibrous tissue, (2) the adenocarcinoma, and (3) the cellular or medullary.

The scirrhus is not an uncommon type and is composed of dense fibrous tissue in which are small irregular nests of cancer cells, each nest containing from 5 to 10 cells. The cytoplasm stains heavily. Mitoses are rare. One gains the impression of very slow-growing, infiltrating type of cancer. Of the five cases showing scirrhus cancer only one shows changes accredited to radium and this change is found only in the periphery. The other four cases do not show any evidence of the effect of radium although two received over 2000 milligram hours of radium.

The adenocarcinomata comprise the largest proportion of specimens. The effect of radium on this type is variable. It is apparently resistant to relatively strong doses of radium, as some of the specimens had large amounts of radiation with little effect while others showed an effect which

corresponded to the amount of radium given. No. 4718 is a case which received 2000 milligram hours in the same area in 9 months. Section through that area shows typical active cancer with moderate connective-tissue stroma. No. 9038 shows after 4000 milligram hours of radium given in 6 weeks a benign adenoma invaded with cancer. The prostate was removed in toto and sections were cut at different levels. Large areas containing solid masses of degenerated cancer cells were seen throughout the section. Here and there was a few masses of cancer cells which appeared perfectly normal in shape and outline. There was no swelling, vacuolization, or granular condition of the cytoplasm. Mitoses were rare. Why these areas remain unaffected when adjacent cancer tissue on all sides shows degenerative changes is an unsettled question. The connective tissue was rather marked in amount, but the benign adenoma was not affected. Twenty-seven of the 33 cases were of the adenocarcinoma type; 7 showed generalized carcinomatous degeneration in various stages. The amount of radium varied from 900 milligram hours to 4000 milligram hours. Of the 20 remaining cases only 8 showed changes in the periphery; while 12 did not show any evidence of degenerative effect from the gamma rays, although these received from 900 to 3000 milligram hours.

The third type or cellular cancer of the prostate is in gross a very soft mucoid, chocolate-colored material. Microscopically it is found to be made up almost wholly of cancer cells interspersed here and there with collections of red blood cells. There is a very small amount of connective-tissue stroma. One case was found among the 33 cases. Fourteen hundred milligram hours of radium were given—but no change due to radium could be discerned from the study of the sections.

Conclusions.

1. A combination of radium and surgery offers a possibility for treatment of cancer of the prostate and seminal vesicles.

2. Operation does not diminish the amount of radium necessary to produce good results.

3. Operation does not increase the possibility of hastening metastases.

4. Histological picture is variable.

5. Radium does not act alike on all cancer tissue.

6. Radium has two distinct actions: one of gradual cell destruction and fibrous displacement and another of necrosis.

7. There are three kinds of cancer of the prostate: (1) scirrhus, (2) adenocarcinoma, (3) cellular or medullary.

REFERENCES

1. Young, Hugh H., and Frontz, William A. Some new methods in the treatment of carcinoma of the lower genito-urinary tract. J. Urol., 1917, i, No. 6.

2. Ibid.

3. Alter, Nicholas M. Histological changes of the different types of carcinoma after exposure to radium rays (Study No. 11). J. M. Research, 1920, xli, 439-456.

TREATMENT OF MALIGNANT DISEASE OF THE PROSTATE AND BLADDER *

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PART I

In the past twenty years, there have been registered in the Urological Department of Johns Hopkins Hospital approximately 450 cases of cancer of the prostate.

Cancer occurs in the same period of life as prostatic adenoma, so that the age of incidence is of little value in the differential diagnosis. Unfortunately, cancer of the prostate seldom produces symptoms until the disease is far progressed. Urinary symptoms, as a rule, are not produced until the vesical orifice or prostatic urethra becomes extensively involved, leading to their contracture. In occasional cases symptoms resulting from metastases are present before the onset of any urinary obstruction.

In early cases of cancer, the patient usually presents himself, not because of symptoms produced by the cancer, but frequently because of symptoms of urinary obstruction resulting from adenoma. In rare cases early cancer is recognized where examinations are made as part of the routine physical examination. In nearly every instance, however, when the patient is first seen, the disease has advanced to the posterior bladder wall or into the region of the seminal vesicles, rendering radical extirpation impossible. In only twenty-one cases out of four hundred was the cancer found confined to the prostate and it was considered possible to excise all of the cancerous tisue. In fourteen cases the radical operation of Young was carried out, and in the remaining seven of the cases a total prostatectomy was done. In this latter group, the growth was well confined to the prostate, thus making possible its complete extirpation without necessitating the removal of the seminal vesicles and neck of the bladder. It is of interest to note that in all of these cases in which a subtotal prostatectomy or complete removal of the prostate with its capsule was carried out, there has been no recurrence of the disease. It should be noted, however, that in all of these cases, it was possible to remove the cancer with a wide margin of healthy tissue. Young has reported in his series of fourteen radical operations a cure of 50 per cent, but this operation is limited in its application to those cases in which the disease has extended only slightly beyond the prostate.

In our experience in 95 per cent of the cases surgery alone is hopeless so far as complete extirpation of the malignant disease is concerned. Therefore, if we are to obtain a greater percentage of cures, some other form of therapy must be developed, which will secure results, either alone or in combination with surgery, with our present available methods of treatment, the most that we can hope to accomplish is the relief of uri-

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nary obstruction or the prevention of its development. Forty per cent of the cases when first seen have either complete retention or obstructive symptoms with a large amount of residual urine. In many of these cases the symptoms resulting from urinary obstructions are distressing and some procedure must be employed to give relief. In 60 per cent only slight or no residual urine is present, and the patient has presented himself principally because of frequency or painful urination. In many of these cases, the symptoms are aggravated and largely produced by an accompanying cystitis.

Radium Therapy

The promising and often enthusiastic reports of the value of radium in the treatment of malignant disease promoted our use of radium in cancer of the prostate. This work was begun in 1915. Since that time, radium has been employed alone or in combination with operation in one hundred fifty cases. Up to eighteen months ago radium was used exclusively through the urethra and per rectum against the prostate and seminal vesicles. A platinum capsule containing 100 mgm. of radium was applied for one hour, this being repeated every second or third day, the radium being applied each time at a separate point so that the applications would overlap as little as possible, and thus minimize the possibility of irritation. From ten to fifteen hours were given per rectum and about five hours per urethram this constituting the first series of treatment. Usually at the end of this time, in many cases considerable rectal irritation was produced, the patients having quite frequent stools with the passage of considerable amounts of mucus. With the first appearance of these symptoms, treatment was discontinued and the patient was asked to report in about two months for a second series. It was usually found in the second series that the amount of radiation which the patient would tolerate without producing marked rectal irritation was distinctly less than in the first series. If possible, some months later the patient was asked to return for a third series. In about 25 per cent of the cases which received 2000 to 2500 mgm. hours per rectum rather distressing rectal symptoms were produced.

Examination of the rectal mucosa in these cases shows a marked thickening and edema with considerable congestion. In some cases ulceration has been noted. The duration of these symptoms after the cessation of treatment usually continues for several months and occasionally for six months or longer. In certain cases developing symptoms of rectal irritation, following the first series of radiation, the resumption of treatment after the disappearance of rectal symptoms is rapidly followed by severe and protracted irritation. In occasional cases the appearance of rectal symptoms is rapidly followed by severe and protracted irritation. In occasional cases the appearance of rectal irritation is delayed for several months after treatment has been discontinued. Local measures directed toward the relief of symptoms have been of little value. Starch enemata have afforded a certain relief in some cases. In our earlier experience in the treatment of these cases per rectum, several very severe radium burns were produced. In one of these a colostomy was carried out because of rectal obstruction, resulting from the intense edema of the rectal tissues. In the other cases the same procedure was done because of severe ulceration with accompanying pain and tenesmus.

During the past eighteen months, we have been needling the prostate in combination with applications per urethram and per rectum. The

needles are inserted through the perineum in the manner advocated by Barringer, 12.5 or 20 mgm. needles of radium element being employed, these being left in the prostatic tissue from fifteen to thirty hours giving a total radiation of from 500 to 1000 mgm. hours at each treatment. The urethra receives a series of radiations totaling about 500 mgm. hours, with about 1000 mgm. hours are given per rectum. One advantage in employing the needles is that it brings the radium in intimate contact with the cancerous tissue and decreases the amount of radiation given per rectum and per urethram, thus decreasing the danger of irritation.

Examination of the prostate after the first series of 1500 to 3000 mgm. hours of radium treatment, usually showed a marked change in the character of the prostate. While it was occasionally decreased in size, the most marked change noticeable was in the consistence of the gland. Instead of being stony hard, it was now rather elastic and of a consistence of hard rubber. The change was frequently so marked that one would not recognize the prostate as cancerous. Although these marked changes occurred in the size and consistence of the prostate, the seminal vesicles seemed usually very much more resistant and the induration persisted there a much longer period of time. While one could not deny the marked change which occurred in the character of the prostate, this change tending to make one rather enthusiastic in the beginning, *it soon became evident that the relief of obstructive symptoms was not proportional to the apparent change in the prostate. In very few cases in which complete retention or a large residual was present was there any relief of obstructive symptoms.* In many of the cases in which the amount of residual decreased or the retention was relieved, the results could frequently be attributed to the use of an intermittent or retention catheter, or to the urethral dilation which the application of the radium entailed. Barringer, in several reports which he has made concerning his experience with cancer of the prostate, has obtained almost identical results. Because of the failure to relieve obstruction in these cases of large residual or complete retention, prostatectomy was carried out in a considerable series, and it was possible then to say to what extent the radium had affected the cancer tissue.

In most cases in which a considerable amount of radium had been employed, the cancer tissue showed microscopically a marked change. Over large areas one would find a complete disappearance of epithelial cells, the connective tissue framework still persisting. In other areas the cancer cells appeared to be shrunken and almost unrecognizable, while in blocks made from other points, the cancer tissue was well preserved. In every case operated upon distinct cancer tissue, apparently unchanged could be found in areas notwithstanding the amount of radiation previously employed.

The failure of radium to secure relief of obstruction when there is complete retention or a large residual urine except in a small percentage of cases will necessitate the employment of other procedures to secure this result. A part of the failure to secure functional results can be attributed to the fact that in a large percentage of cases the carcinoma is associated with hypertrophy, the radium having little or no effect on adenomatous lobes.

The value of a modified perineal prostatectomy in relieving the obstructive symptoms, even in advanced cases of cancer of the prostate, has long been realized in our clinic.

Of the two hundred fifty cases of cancer of the prostate seen in the Urological Clinic up to the year 1915, in one hundred of these perineal prostatectomy was carried out. In 75 per cent of these there was no return of obstruction up to the time of the patient's death, many of these patients living a number of years. Of these one hundred cases, there was an operative mortality of 3 per cent. In seventy cases it has been possible to secure information concerning the duration of life. Sixteen of these lived less than six months, fifteen between six months and a year; twelve between one and two years; ten from two to three years, and seventeen three years or more. Of these seventeen cases, nine lived between three and fours years. Of the remaining eight cases, 2 lived about four and one-half years, two six years, two nine years and two fourteen years.

The average time of closure following operation differs not at all from the time of closure in the benign hypertrophy cases. In seven cases, a fistula persisted up to the time of death. In none of these one hundred cases, in which prostatectomy was carried out, was anything more than relief of obstruction contemplated, and there was no attempt or thought of eradicating the disease. The low mortality and the relief of distressing obstructive symptoms secured by this operation, relief in the majority of cases extending up to the time of death, is a sufficient justification for this operative procedure

When a patient presents himself with an advanced carcinoma of the prostate, a large residual urine or complete retention, he is prepared for prostatectomy in a manner similar to that used where prostatectomy for benign adenomas is contemplated. The operation is, of course, not advised where there is advanced cachexia or where the condition of the patient is such that a very short period of life is expected. In such cases palliative measures are adopted to secure for the patient as great comfort as possible. In such cases, except in dire necessity, operative procedures are not carried out.

Technique

The patient is placed in an exaggerated lithotomy position and the membraneous urethra exposed according to the technique employed by Young in perineal prostatectomy. In many cases the membranous urethra will be found markedly thickened because of the extension of the cancer to the peri-membranous tissue. The extension adds but slight difficulty to the proper opening of the membranous urethra which is carried out on a sound. The introduction of the tractor will be found difficult in many cases, because of the extreme contraction of the urethra, and its introduction will necessitate frequently marked divulsion of the prostatic urethra to aid its insertion. A straight tractor such as was devised by Wilder will be found easy of introduction in these cases. Usually the levator muscles and rectum will be found quite adherent to the posterior lobe of the prostate, and an attempt to secure a dissection as is carried out in exposing the benign prostate, will lead to serious danger of rectal injury. To obviate this complication the following procedure should be employed: The levator muscles are dissected back from a small area at the apex of the prostate and a short "V" shaped incision is made into the prostatic tissue at this point, enabling one to carry back the levator muscle and rectum with a substratum of cancer tissue attached to them. From this exposure of the prostatic cancer, by means of a sharp curet aided by scissors or rongeur, the center of the

prostate is removed, usually en morecellment. As the cause of obstruction is usually the contraction of the vesical orifice or formation of lobular carcinomatous masses at the level of the sphincter, extreme care should be employed to remove most of the tissue from this area. The curettage or enucleation should be continued until a widely dilated vesical orifice is obtained. In some cases when the cancer is associated with adenomatous lobes, the interior of the prostate can be enucleated in one piece or in large masses. After the obstruction has been relieved a large tube is introduced into the bladder through the opening in the membranous urethra and apex of the prostate. Hemorrhage is controlled by gauze packed around the tube. Needles containing radium element or emanation are now inserted into the shell of cancer which has been left. Special preference should be given to the neighborhood of the vesical orifice when this is extensively involved. A radiation equivalent to 1000 mgm. hours is usually employed. This amount has not been followed by any marked symptoms of irritation or any evident systemic toxic symptoms. It is of interest to note that the hemorrhage where this technique is employed is rarely severe and easily controllable by slight packing. The hemorrhage on the average is distinctly less than in the cases of benign hypertrophy and the shock connected with the operation carried out by the above technique is no greater than that associated with the ordinary external urethrotomy.

There is a fair-sized series of case in which the growth has advanced to the posterior bladder wall and base of the seminal vesicles, too far for complete extirpation by the radical resection of the neck of the bladder, vesicles and prostate. In a series of five cases in this group, the writer has carried out a radical operation which consists in complete removal of the prostate and seminal vesicles without the destruction of the internal sphincter (see plates 1 to 8). In these cases it is possible to remove practically all of the cancer except a slight extension on the posterior bladder wall.

In view of the definite action which radium has on cancer of the prostate when used over a long period and in sufficient quantities, it seemed to me possible that after the removal of the main mass of cancer tissue, radium therapy might cause complete disappearance of the small areas of cancer which would remain behind. In this small series, after complete removal of the prostate and seminal vesicles, radium was placed in position back of the bladder and beneath the vesical orifice, a total of 600 to 1000 mgm. hours being given in one application. In none of these cases was there any marked irritation produced by the radium. Of these five cases, two died within a year of metastases, one had a local recurrence, and two are living and well for a period of three years. These two cases, on rectal examination, show no evidence of carcinoma.

Results obtained by a comparatively radical operation, combined with radium therapy, would seem to indicate the possibility of radical cure in a larger number of cases than could be accomplished by any operative procedure alone.

Summary

The results obtained in the treatment of cancer of the prostate by various procedures or combination of procedures would seem to indicate the following:

Where the cancer is localized in the prostate and has not invaded the posterior bladder wall and seminal vesicles, the radical operation advised

by Young is definitely indicated, provided the age of the patient is not too great or there are not present other contra-indications rendering a radical operation extremely dangerous. Where complete extirpation can be accomplished, a large percentage of ultimate cures can be anticipated, as, at this stage of the disease, metastases rarely occur.

The operation, however, will not have a wide application until earlier cases of cancer are seen by the surgeon. Where the malignancy is confined to one lobe and has not invaded the posterior bladder wall, but is well confined to the prostate, complete extirpation of the lobe or lobes, including the capsule, has resulted in permanent cure in six cases in which this procedure was carried out.

The technique of complete extirpation is very little, if any, more difficulty than the ordinary perineal prostatectomy. *In the series of cases in which marked obstruction or complete retention is present, the functional results obtained by radium therapy have been disappointing notwithstanding the marked change which frequently occurs in the prostate and vesicles.* In practically all of these cases, the disease is so far advanced that we can hope for nothing except relief of symptoms, and radium alone apparently does not accomplish this in a sufficiently large percentage to warrant the employment of radium alone. Where marked obstruction or retention is present, a conservative perineal prostatectomy gives excellent functional results with a very low mortality. It carried out with the technique described above, the procedure will not be found dificult, nor will it be attended by any serious complications such as recto-urethral fistula, etc. Closure of the wound will be almost as rapid as following a simple urethrotomy.

At the time of operation, after sufficient tissue has been removed to relieve the obstruction, radium needles are inserted into the cancerous tissue. After the closure of the wound, the patient receives a series of radium treatments with the idea of delaying a subsequent development of obstruction.

In about 50 per cent of cases, operative procedures will be unnecessary as little or no obstruction to urination is present. Radium probably will prove extremely valuable in this group of cases, not so much for the cure of the cancer as in preventing the development of urinary obstruction later. In practically all of our cases in which slight or no obstruction was present when the patient was first seen and in whom radium was employed, no serious obstruction later developed during the life of the patient. While radium has not accomplished all that was hoped for in the cure of cancer of the prostate, it still has a very definite field of usefulness. Its chief field of application will apparently prove to be in that group of cases which have advanced cancer without urinary obstruction in helping to prevent the development of urinary obstruction with its attending distressing symptoms. Radium cannot be considered as replacing operative procedures but in many cases serving only as a valuable adjunct in the treatment of cancer of the prostate. Obviously the application of radium to the prostate can have no influence on the pains due to metastasis.

PART II

The introduction of the cystoscope, making possible the early diagnosis of bladder tumors, has enabled the surgeon to attempt their excision. Until the cystoscope began to be employed there was no diagnosis of bladder tumor made in the Johns Hopkins Hospital except

where a suprapubic cystotomy was done because of intolerable bladder symptoms, the operator not infrequently finding a bladder filled with cancer.

With the possibility of early diagnosis with the aid of the cystoscope, the surgeon began to direct his attention to the destruction or excision of these vesical neoplasms. At first, through a suprapubic exposure of the bladder the removal of these tumors was accomplished principally by means of clamp and cautery or by destruction with the cautery alone. A favorite measure was to place a clamp across the pedunculated tumor and then with the cautery blade cut across the pedicle. The more extensive infiltrating growths were cauterized with varying degrees of intensity. The surgeon soon found, however, that practically no results were obtained where the growths were infiltrating and extensive, and that notwithstanding his greatest care in the removal of the more pedunculated and localized growths, he almost invariably, or at least in the vast majority of instances, had to contend with subsequent recurrences. It was frequently noted that where originally there had been only one tumor, the surgeon subsequently found the bladder studded with recurrent growths, and not infrequently the suprapubic tract itself became the seat of implanted tumor. Sometimes a second and third suprapubic excision was carried out, but the end result was always the same and each succeeding operation found conditions worse.

In 1909 in the symposium before the International Congress, the vast majority of surgeons had about come to the conclusion that patients, as a rule, live longer without operation; that operation was only advisable where there was a definite carcinoma which could be resected, and that only in such cases should surgery be attempted. The results obtained by most surgeons were so discouraging that very few recommend ed operation with any degree of enthusiasm. The surgeon had no difficulty in thoroughly and effectively destroying the pedunculated papillary tumor. He could not prevent however its recurrence, and when this resulted, he had no means other than surgery to remove it.

While removal of the superficial or pedunculated papillary tumors could be successfully carried out by means of the cautery, it soon became evident that this was not an efficient means of removing infiltrating growths. In the infiltrating type of tumor the radical removal of the area of bladder wall involved was the only treatment which was followed by satisfactory results. It was the common experience of the surgeon that when he resected for malignant growths, this procedure being more or less limited to definite cases of cancer, local recurrences were less frequent than in those cases in which comparatively benign and seemingly innocent tumors had been destroyed by the cautery. This has been our experience. This difference of opinion was so striking that some surgeons boldly advocated that resection, where at all possible, should be carried out in every case of vesical tumors.

While surgeons were obtaining such poor end results, Nitze, by means of his ingenious operating cystoscope was securing results incomparably superior to anything that surgery had up to that time accomplished. He first secured pieces of tumor for microsopic examination, and if the tissue proved to be cancerous, he did not attempt its removal endovesically. If, however, the tumor was not cancerous, he removed it by this means. The percentage of tumors which he was able to remove through his operating cystoscope and his end results compare almost identically with results obtained by the methods employed

today. Apparently the type of tumor which we can today remove by means of fulguration he succeeded in destroying by means of his ingenious cauteries and wire snares. With the introduction of fulguration by Beer in 1910 a new era in the treatment of bladder tumors was begun. The excellent results obtained in certain tumors and failure of the treatment in others led to very careful histologic studies and it soon became evident that fulguration was only effective in benign and malignant papilloma and that it failed to remove the true papillary or infiltrating carcinoma.

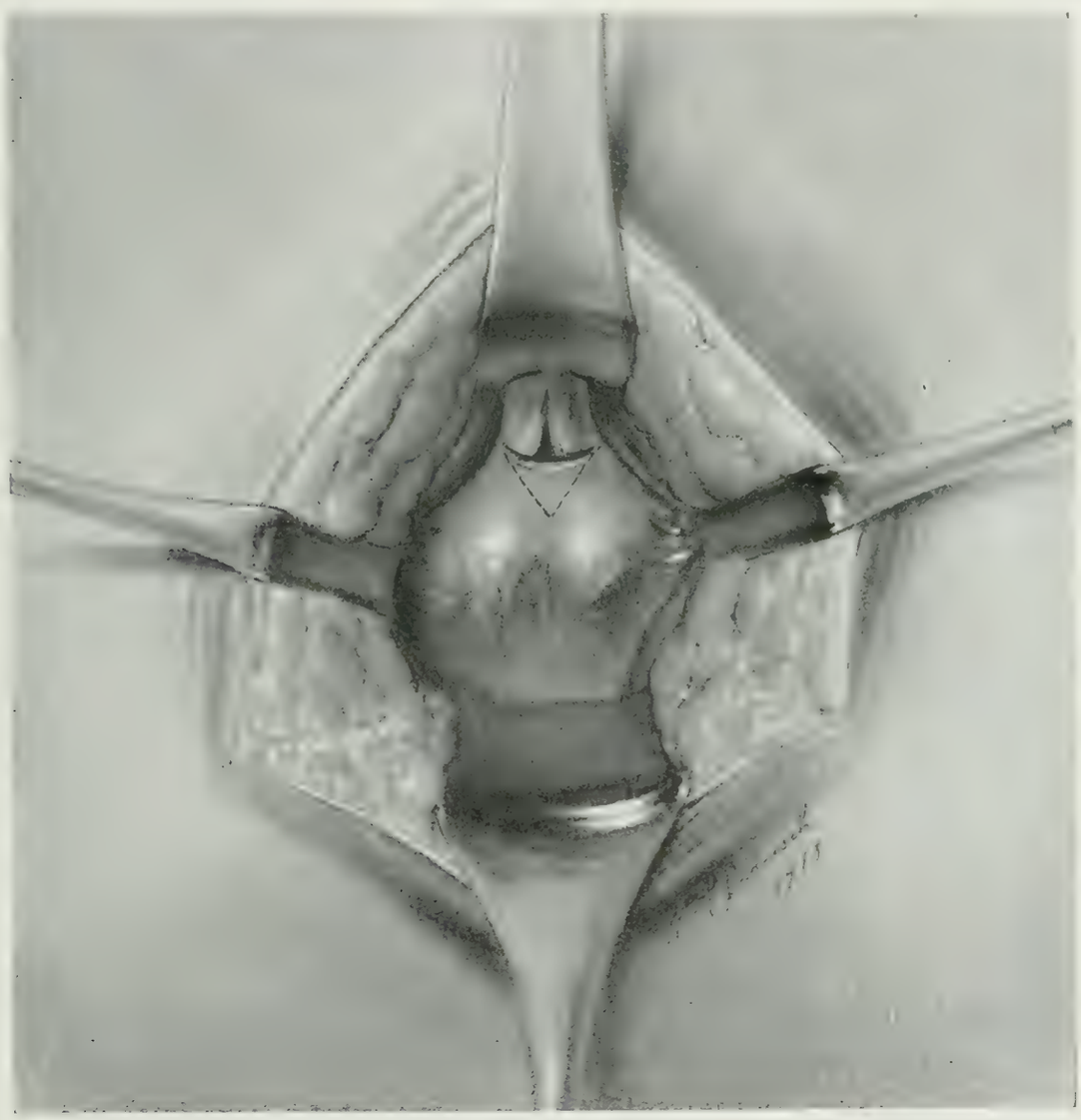

PLATE 1

The prostate has been exposed and the membranous urethra opened. The urethra is now divided, the dotted line indicating the line of incision on the anterior urethral wall.

In a study made some years ago, we were able to show a recurrence in 40 per cent. of the cases within a period of three years. In all these cases the primary tumor had been completely and entirely removed by means of fulguration. The great majority of the recurrences were observed within the first year. In thirty-one of our cases in which papillary tumors had been removed by suprapubic cauterization, recurrences were noted in twenty-five; of the six remaining cases, no recurrence was present in six months in two; one was well two years; one

three years; one five years and one ten years. The patient who was free of recurrence for ten years developed, some months later, a small papilloma on the right lateral wall which responded promptly to fulgu-

PLATE 2

A cross section of plate 1. The dotted line indicates the line of excision of the prostate and seminal vesicles.

ration. He had no recurrence two years later. It can be seen from these figures that recurrence following removal by means of fulguration is distinctly less frequent than following suprapubic removal of the same

type of tumor. Furthermore, it has been our experience that where the primary tumor has been removed by means of fulguration, the recurrent tumor, if seen early, will respond to this treatment. The results obtained

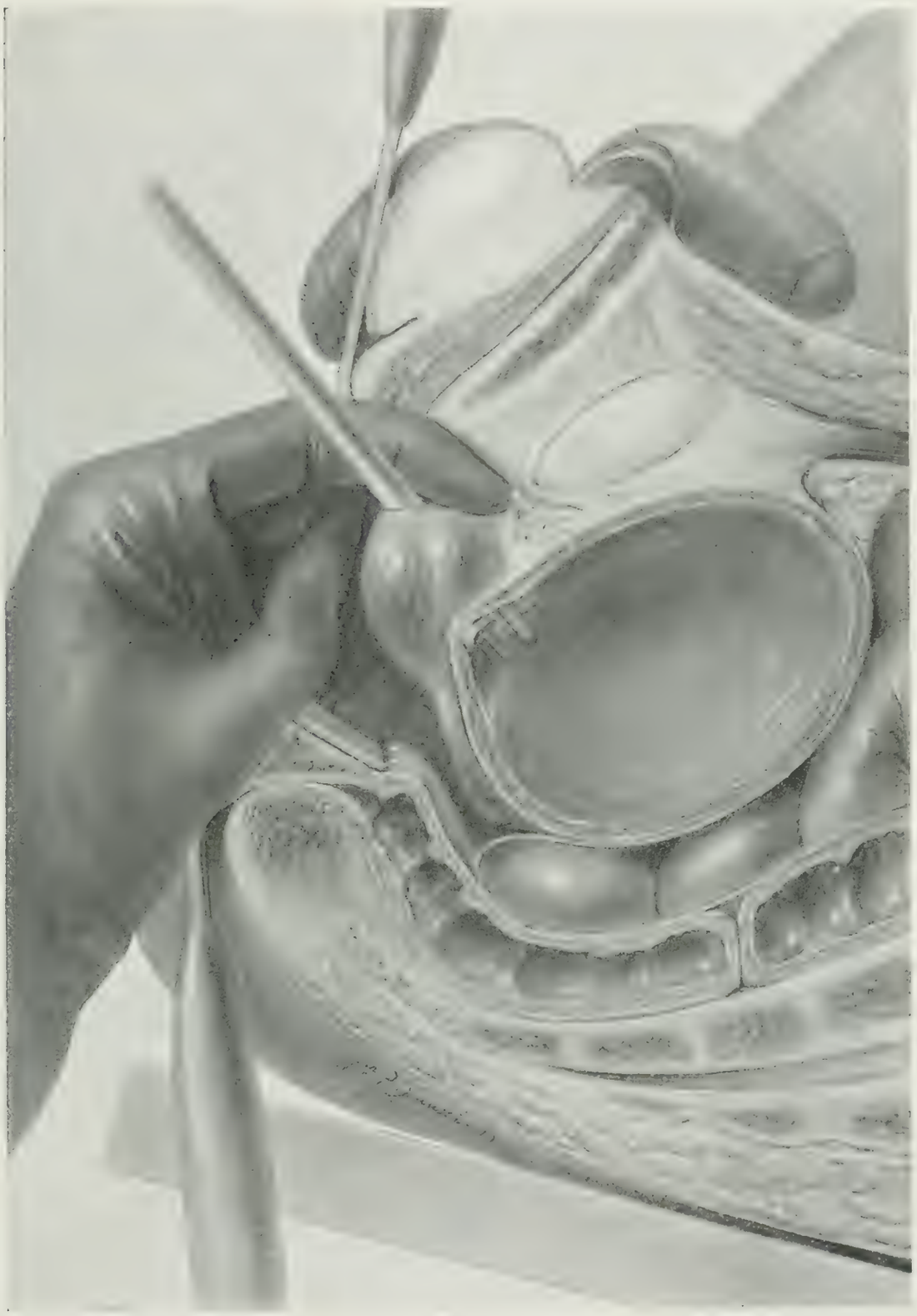

PLATE 3

The urethra has been divided, the prostate drawn downward and the freeing of the anterior surface of the prostate begun.

by fulguration in the tumors suitable for this form of treatment are really so encouraging that little more can be expected, and the results

are incomparably superior to any result which can be obtained by operative procedure. About 40 per cent. of all cases of bladder tumor presenting themselves in our clinic belong to the benign or malignant type suitable for fulguration. This, it is apparent, leaves a great many tumors unsuitable for this form of therapy.

Radium. In 1915 we began the use of radium in the treatment of bladder tumors. Practically all tumors, whether papilloma or carcino-

PLATE 4

The prostate is pulled downward and its anterior surface freed up to the point of its attachment to the bladder wall.

ma, were subjected to radium therapy. It was soon found that all of the papillomata responded to radiation and disappeared with varying amounts of treatment, depending upon the size of the tumor.

Technique. By means of a special cystoscope 100 milligrams of radium were carried into the bladder which was previously distended with fluid, and then under direct vision the radium was placed against the tumor mass. It was usually left in position for one hour and the treatment was repeated about every second or third day. The frequency and the period of duration of any one treatment naturally varied some-

what with the tolerance of the individual. This accurate placing of the radium against the tumor mass is very essential, because to effect the tumor favorably and cause its disapearance, frequently required more radium than would ordinarily be sufficient to produce a severe burn of the normal bladder mucosa. This can largely be avoided by accurately placing the radium directly against the tumor and keeping the normal bladder wall distant by means of a quantity of fluid in the bladder

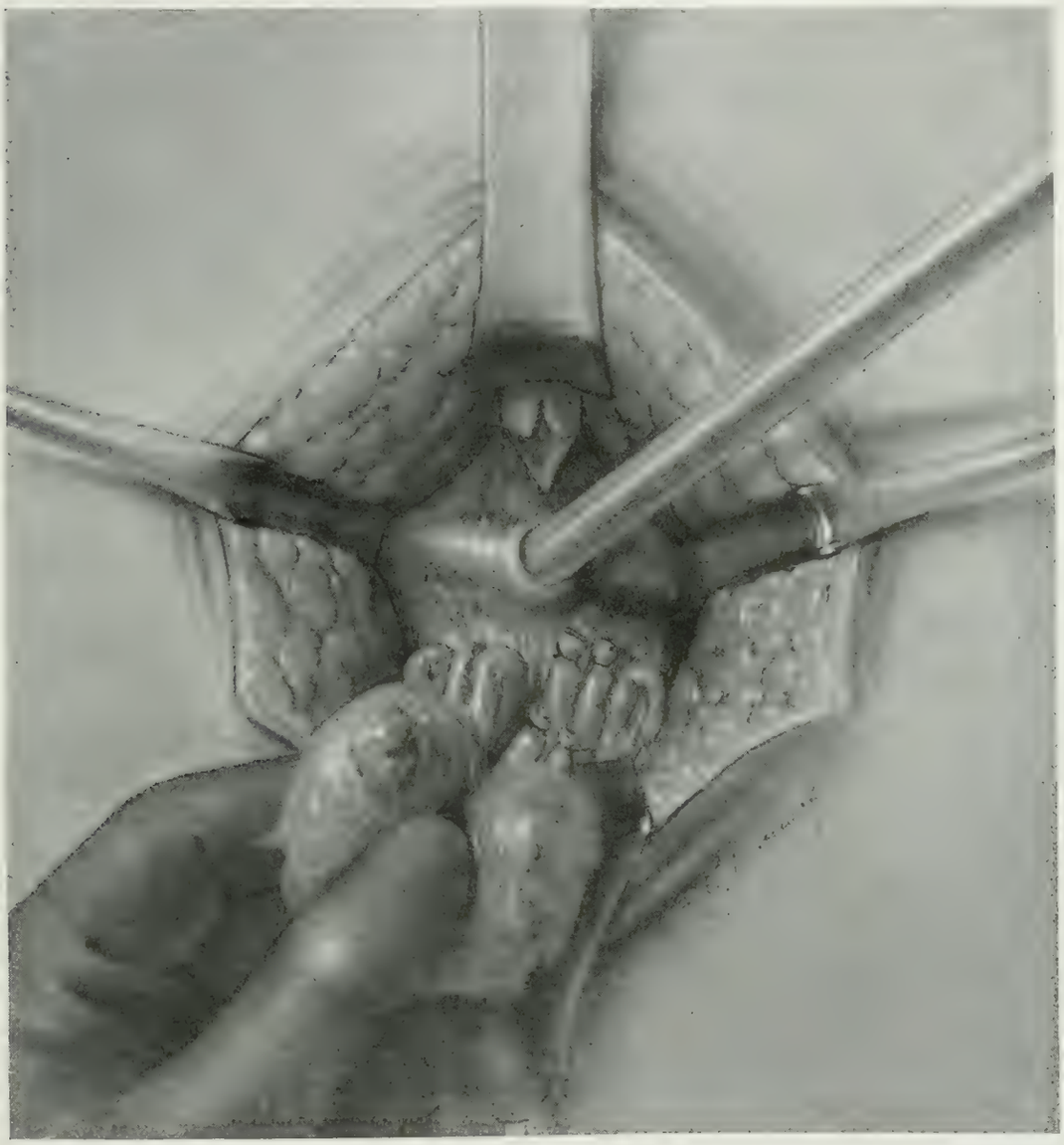

PLATE 5

The prostate has been separated from the bladder, this being easily accomplished. The anterior commissure has been divided and the prostate freed from the tractor. In this instance the vesicles and vas are not removed.

cavity. We have in some instances given 2000 to 3000 mgm. hours to infiltrating growths without seriously affecting the surrounding bladder mucosa.

Early in our work, it was found that some papillary tumors which seemed extremely resistant to fulguration treatment, responded very promptly after a small amount of radiation. Consequently, it has been a habit in our clinic to radiate most tumors, even those which subsequently will be treated by fulguration.

Radium has been employed in the past six years in our clinic in 150

cases of bladder tumor, either alone, in combination with fulguration or operation. It has been found that radium will destroy all papillary tumors which will be affected by fulguration. It is rather interesting to note that in one case with multiple tumors on the trigone, most of which disappeared under intensive radiation, one seemed to be resistant, and withstood enormous doses of radium over a period of many months.

PLATE 6

Showing complete prostatectomy with seminal vesiculectomy.

This tumor, although apparently withstanding intensive radium treatment, when subsequently fulgurated, responded most promptly and disappeared as quickly as the ordinary benign papilloma. We have no explanation of this peculiar resistance.

Our results with radium in the treatment of extensive infiltrating carcinomas have been most discouraging. Although in many instances, many hundred milligram hours of radium application were given directly over the tumor area, in no instance was the tumor, which was

distinctly infiltrating, cured by radium therapy. Ofttimes, very malignant looking tumors, which were apparently only slightly infiltrating have disappeared under the radium action.

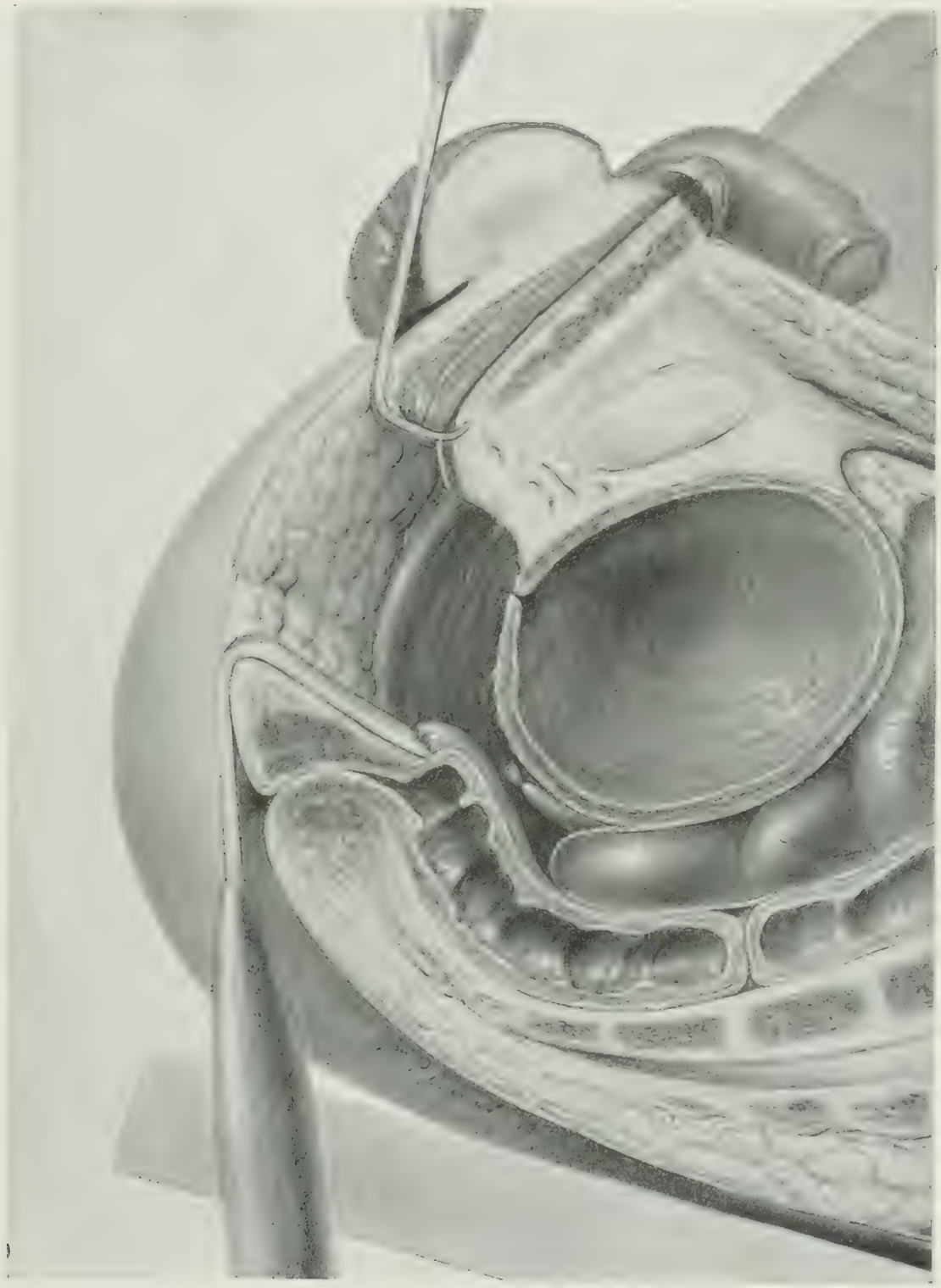

PLATE 7

Cross section showing end of divided urethra. The prostate and seminal vesicles have been completely removed, leaving the internal sphincter intact.

About 50 per cent. of all tumors occur in the region of the ureteral orifices where infiltration, if present can be detected by rectal palpation. In not a single instance in which a tumor associated with induration,

which could be detected on palpation, has there been a disappearance of the tumor or a cure of the tumor effected.

During the past six months, following the suggestion of Barringer, in cases in which resection is not feasible, we have been opening the bladder and implanting emanation tubes deeply in the tumor tissue. So far, our results have been discouraging. It is only fair to say, however, that all of these cases in which this form of therapy was adopted were very extensive. In no case so far, in which we failed to effect the cure of tumor by intensive surface application to the tumor area, have we succeeded in curing it by infiltration with emanation or multiple radium needles. Our experience, however, is too limited to draw any positive conclusions regarding the benefit to be derived from this procedure. Although radium in our hands fails to effect a cure in the extensive infiltrating growths, there is a large group of papillary carcinoma in which only superficial infiltration is present, which are satisfactorily handled with radium. Frequently these tumors are multiple or creep superficially along the mucous membrane surface spreading over large areas. This is a group of tumors which will not respond to fulguration and are mostly inoperable. When the bladder is opened suprapubically in this type of case and an attempt made to destroy the tumor or tumors, recurrence and implantations are most apt to occur. It is in this group of tumors in which radium has given us our most brilliant results—a group of tumors in which fulguration fails and surgery is useless. In these tumor cases it is inadvisable to open the bladder, and we have found it preferable to direct the radium therapy against the surface of the tumor, accurately placing the radium on the tumor surface itself. In this particular group, recurrences are frequent and rapid, and one has to treat frequently recurrences in these cases at short intervals over a period of several years. In one such case, at least fifty tumors were removed during a period of two years. The patient now has had no evidence of recurrence during the past six months.

Tumors Anterior to Vesical Orifice

It has been our experience that tumors in this location should receive surgical treatment, no matter to which group they belong, because it is impossible with any of our present cystoscopes to treat accurately and apply therapy to tumors in this position. In at least three instances we have allowed tumors which apparently in the beginning were comparatively benign, to go on to infiltrating carcinoma before it was discovered that this had occurred. I would recommend very strongly where tumors are partly visible in this position to institute surgical removal. If the tumor is papillomatous, it can be destroyed with the cautery or resection can be carried out. Tumors in this position are not suitable for endovesical treatment and are extremely favorable for operative treatment.

Metastases. It is surprising to what extent tumors of the bladder may progress without the recurrence of metastases. We have been astonished in many cases with extensive malignant tumors of the bladder dying, because of sepsis, renal or some intercurrent disease, to find no demonstrable metastases. In twenty-seven cases of bladder tumor coming to autopsy, in which the growths were extensive and true carcinoma, in only three was the pathologist able to demonstrate metastasis. The slowness and the late date of occurrence of metastases would bespeak

an attempt at radical operation, even in very extensive tumors, where it is at all possible to remove the local growth. If the local growth be removed, the prognosis from a metastatic standpoint will apparently be good. In three of our cases the primary tumor disappeared very promptly and rapidly under the influence of fulguration. The patients were seen from time to time and no evidence of re-formation of papillary tumor was noted. One of these patients developed subsequently at the site of the former tumor what was apparently a severe cystitis, the mucous membrane being very red, uneven and in places slightly ulcerated. The other two patients developed similar mucous membrane changes but at a point far removed from the original tumor, in both instances being in the opposite half of the bladder.

Case 1. This patient, a male, aged 47, was admitted March 16, 1916, the cystoscopy showing a large papillary tumor back of the right ureteral orifice. This was vigorously fulgurated on three occasions which resulted in a rapid disappearance of the tumor. It was the operator's impression that the tumor belonged to the benign type of papilloma. Subsequent examinations showed the mucous membrane at the site of the former tumor to be quite edematous, very red and somewhat uneven. In August, 1916, five months after the disappearance of the tumor, recurrence was noted behind the right ureteral orifice. This was smooth and there was slight tendency to sloughing. Some edema of the mucosa adjacent to the tumor was also noted. About 200 mgm. hours of radium were applied to the tumor, which disappeared quite rapidly. Examination four months later showed considerable reddening and edema of the mucosa at the site of the recurrence. No tumor, however, was visible, and rectal examination showed no induration of the bladder wall. The patient was next seen in July, 1917, at which time the edema of the mucosa was still present without any definite tumor being noted. Rectal examination at this time, however, showed a great deal of induration in the region of the right seminal vesicle and the base of the prostate.

Case 2. Patient, male, aged 55, was first seen in March, 1916. Cystoscopy showed an irregular papillary tumor back of the left ureter. This was fulgurated and rapidly disappeared. Examination seven months later showed the region of the bladder occupied by the original tumor to be normal. Back of the right ureter there was noted a localized area about 2 cm. in diameter in which the mucosa was red, edematous and uneven. There was no evidence of tumor. The area gradually increased in size and it finally became apparent that there was present a carcinoma in the bladder wall beneath the mucosa, there being no projecting tumor. Although radium was applied directly to the area the spread of the disease was not controlled and the entire bladder wall gradually became involved.

Case 3. Patient, male, aged 44, was first seen in November, 1914, complaining of frequency and burning on urination. On cystoscopy there was found in the region of the left ureter three papillomatous masses, the largest being about 3 cm. in diameter. External to the right ureter the mucosa was extremely red and slightly elevated. This was thought to be an area of localized cystis. The tumors around the left ureter were fulgurated and promptly disappeared. Three months later the area had increased considerably in size. A rongeur specimen obtained from this area showed superficially a chronic inflammatory process, while the deeper part of the section was typical cancer. Radium applications were made to this area without checking the spread of the disease, the entire bladder gradually becoming involved.

The last two cases cited would seem to indicate that it is possible for metastasis to occur in the bladder wall at some distance from the primary tumor as well as immediately beneath the tumor. There seems no plausible explanation of the carcinoma beneath an infected mucosa unless we admit that this represents a metastasis.

An observation, similar to the three cases cited above, has been made in a case treated with radium. A large papillary tumor back of the left ureter disappeared under application of radium. A few months later, at the site of the original tumor, there was noted some reddening and

ulceration which was at first thought to be a radium reaction. It was subsequently discovered that this apparent radium burn was really an infiltrating tumor of the bladder wall, presenting a picture similar to the cases cited above. These cases represent a metastasis to the bladder wall. While many cases of very extensive cancer of the bladder occur without there being present demonstrated metastases, in occasional instances very small pedunculated papillomata may result in metastases. In three of our cases in which small papillary tumors were destroyed by fulguration, and in which no recurrence of the tumor was noted in the bladder, bone metastases subsequently developed. One metastased to the femur, one to the clavicle, one to the spine. In a limited number of cases it seems that the tumor may metastasize to the bladder wall itself.

Buerger has reported a case in which an apparently innocent pedunculated tumor removed by resection showed in the bladder wall metastatic cancer cells. A similar case has been observed by us. This patient, a man aged 50, had a large papillary tumor on the left postero-lateral wall just back of the trigone. Histologically the tumor was a definitely malignant papilloma, and there was no evidence cystoscopically of infiltration of the bladder wall. The tumor disappeared under a series of radium treatments, leaving a slight reddening and irritation of the mucosa at the site of the former tumor. About two months after the tumor had disappeared, the patient was killed in an automobile accident. Autopsy revealed a normal bladder with the exception of slight ulceration and reddening at the site of the former tumor, evidently the effect of the radium. There was no visible evidence of tumor. Histological sections made from this area showed a superficial zone of inflammation but no surface tumor. In the muscular layer, however, there was discovered a small nest of typical cancer cells, which was undoubtedly metastasis, there being no other evidence of tumor.

Summary. Fulguration should be the method of choice in all benign and malignant papillomata which can be reached by endovesical means. Where the tumors are resistant to fulguration or are papillary carcinoma, non-infiltrating or superficially infiltrating, radium will give uniformly good results, and the results will be obtained by surface applications to the tumors. Where the tumors are deeply and distinctly infiltrating but sufficiently localized so that resection could be carried out and the growth removed with a definite healthy margin of tissue, this procedure should be employed and radium therapy not depended upon. Where, following the removal of the growth, the operator feels that possibly he has not given sufficient margin at any one point, radium should be inserted in the contiguous tissue. In the very extensive cases of carcinoma in which it is impossible to satisfactorily carry out endovesical treatment with radium, it is our custom now to open the bladder suprapubically, destroy as much as possible of the tumor or tumors with the actual cautery, and then implant radium emanation tubes approximately at 1 to 2 cm. distant from each other. What is to be expected from radium applied in this way in these perfectly hopeless cases it is too soon to pass judgment. So far, our results in these otherwise hopeless cases have not been very brilliant.

THE CYSTOSCOPIC APPLICATION OF RADIUM

By Leo Buerger, M. D.
of New York City

In our own work with radium in the treatment of carcinoma of the bladder, the best results have been obtained with the use of radium emanations introduced through a suprapubic incision.† Where, for particular reasons, intravesical application is advisable either in the preparation for future cystoscopic work, or as a method of preference, emanations are also considered to possess the greatest advantages. They can be easily inserted through the author's operating cystoscope.

However, this ideal procedure is available to but very few urologists. It has been my purpose to evolve a procedure that would bring an intensive and efficacious method of applying radium within the reach of the cystoscopist, to perfect a method that will eliminate the necessity of leaving the cystoscope in the bladder, and thus permit of the prolongation of radium contact over a period of many hours without excessive discomfort to the patient.

THE AUTHOR'S METHOD

The armamentarium which has been successfully employed by me is simple, as also the technic of inserting the radium. It includes:

First—Special radium needles.*

Second—Special applicators for the insertion of the needles into the growth,** and

Third—Either the author's operating cystoscope, a direct or oblique vision cystoscope, or the author's radium cystoscope.

The radium needles. Two sizes and types are recommended, steel needles containing 20 mg. each, and a platinum hollow needle enclosing approximately 50 mg. of radium. These have been especially constructed and are of minimum length, so as to be easily introduced either by means of an attachable wire stem or a special spiral applicator.

The needles (1) are composed of two parts, the needle point with shaft and a detachable eye (Fig. 1b). This arrangement permits of the two methods of introduction, namely, in a spiral applicator or Fig 2, with a wire shank (Fig. 3).

The needle point is short and is an integral part of the radium chamber, its proximal end being provided with a female screw thread. This may receive either the eye end, or the male portion of a wire applicator. Thus, such a needle may be introduced into a growth either with an attached wire shank (Fig. 3), or as a complete needle whose eye receives a fine wire retainer. (Fig. 4.)

The applicators. Two types of introducer or applicator have been found useful. One of these is a spiral flexible wire shank (30 cm. long) whose distal end is furnished with a metallic cup for the reception of the eye end of the radium needle (Fig. 2) and whose proximal end is fitted with a metallic enlargement for the insertion of a rubber

†With the co-operation of Dr. I. Levin, New York.

*Constructed for me by the Radium Chemical Co. of Pittsburgh, Pa.

**Executed by the Wappler Electric Mfg. Co., according to my designs.

catheter or nipple. The metallic cup is an incomplete cylinder having a longitudinal slot or an aperture through which the wire may slip or emerge (Fig. 5 A B C). The needle is threaded with fine piano wire doubled on itself and long enough to emerge three or four inches beyond the catheter outlet. Or less rigid, finer wire twisted after being

Fig. 1.—Radium needle; on the left, shaft; on the right, eye.

Fig. 2.—Flexible spiral applicator containing fine mandarin which is used to facilitate expulsion of the needle.

threaded will also be found useful. By means of this wire, the needles may be subsequently withdrawn.

Just before insertion into the cystoscope, the needle is placed into the metallic cap (Fig. 5 E). The wire emerges through the slot or

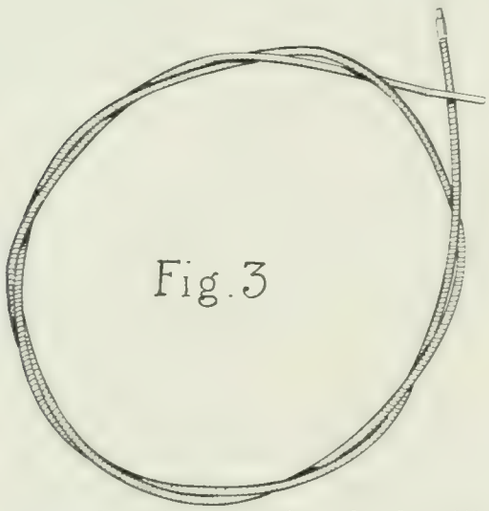

Fig. 3.—Flexible wire shank with screw thread to fit into female receptacle of needle.

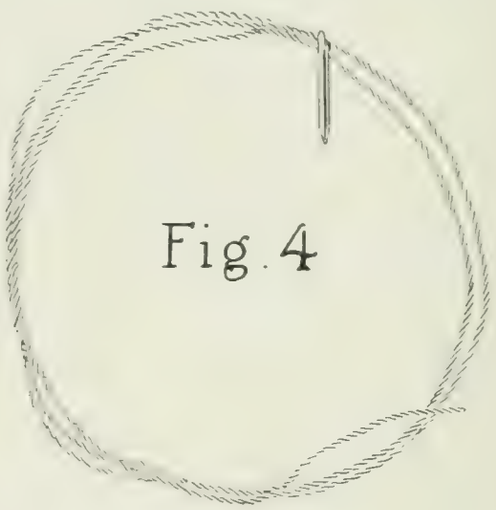

Fig. 4.—Needle threaded with wire.

aperture and passes alongside of the spiral shank, and through the rubber nipple at the catheter outlet. A slight pull on this wire suffices to retain the needle in its socket, or the retaining wire may be fastened to the spiral by an appropriate screw clamp.

When this variety of applicator is employed, our aim is to withdraw it, leaving the needle with the wire *in situ*.

The second type of applicator is intended for those who may find some difficulty in mastering the technic of withdrawal. It consists of a spiral stem with a male thread that fits into the female receptacle of the needle, the eye of which *must be removed* before attachment is made. Although this type may appear easiest to employ particularly as far as withdrawal of the cystoscope is concerned, it carries with it this disadvantage that a larger stem must be retained in the urethra. This may be objectionable in the male, in that it tends to displace the needle out of the growth.

A third applicator is patterned after the first, differing only in the size of its socket which is designed to carry one 50 mg. needle of radium.

For those who prefer the simultaneous introduction of two twenty milligram needles, a special applicator with a broader receptacle may be found useful (Fig. 5 C).

The cystoscope. For special processes we have devised a combination direct type of cystoscope* in which an oblique vision or right angle vision telescope can be inserted. In addition, a radium cystoscope has been devised by us to meet the requirements of tumors that are almost inaccessible to the usual varieties of cystoscope.

Technique. The application of 20 mgm. needles. After localizing the growth and after the diagnosis of carcinoma has been established, one or two needles is prepared, each being threaded with fine wire, doubled and twisted on itself, of a length sufficient to emerge some two inches from the spiral applicator, each being placed into the socket or receptacle of the spiral applicator, the wire emerging through the slit or

Fig. 5

Fig. 5.—Set of applicators.

a—applicator for 20 mg. needle.

b—applicator for 50 mg. needle.

c—applicator for two 20 mg. needles team fashion.

e—20 mg. needle threaded and inserted into cup or receptacle of applicator a.

aperture and affixed to the shank a short distance from the distal end by an appropriate means. Such an applicator with a single radium needle is passed into the telescope, the escape of the fluid at the catheter outlet being prevented by the large nipple, and through the spiral by a small catheter nipple.

The procedure of plunging the needle into the growth must vary depending upon the type of growth at hand, its size and configuration. Thus, we may desire a tangential application, or one perpendicular to the surface. Having introduced the radium needle almost to the eye end, the next step is to release the needle and remove the wire applicator.

*Executed by the Wappler Electric Manufacturing Co., N. Y.

In doing this we must be careful to prevent dislodgment of the needle as the deflector is released. Whenever deflection is employed for purposes of introduction, its amount must be carefully noted so that a reciprocal motion of the cystoscope may be employed when the lid is put down. For, to release the lid without a complimentary motion of the shaft of the cystoscope may result in a recoil of the wire applicator with consequent pulling out or tearing of the needle through the tumor mass.

Having therefore, moved the beak of the cystoscope towards the tumor as we lay the lid down, we are then in the position to remove the spiral. In doing this we must simultaneously introduce the wire retainer as we withdraw the spiral applicator loosened.

If but one needle is to remain in the tumor, the telescope is removed first and the sheath follows.

We have frequently resorted to a checking up procedure to verify the situation of the needle after the removal of the cystoscope by the introduction of a small instrument of sixteen or seventeen Fr calibre, threaded over the wire as it emerges from the uretha. If a second needle is to be inserted, a repetion of the technique is made, the wire retainer of the first needle being allowed to emerge through a special hole in the large rubber tip.

Care must be exercised to prevent dislodgment of the needle already implanted. By leaving enough slack in the bladder, an inadvertent tug on the wire will not be transmitted to the needle itself.

RADIUM IN CANCER OF THE BLADDER*

By George Gilbert Smith, M.D., F.A.C.S., Boston

From the Collis P. Huntington Memorial Hospital, Boston.

The treatment of cancer of the bladder by surgical measures alone has, in a rather small proportion of cases, given satisfactory results. In the greater proportion by far, the growth has recurred and all that remained was to ease with morphine the patient's decline. This statement, I think, will be accepted as true by every genito-urinary surgeon of experience.

During the years 1910 to 1915, the acquisition of radium by a number of hospitals and individuals aroused a general interest among urologists as to the value of the element in the management of malignant growth of the bladder. Could radium be used as a substitute for surgery? Was its employment as an aid to surgery productive of results

In 1916, the Huntington Hospital in Boston began the use of radium in cancer of the bladder. From September, 1916, to January 1, 1921, 24 cases were treated with radium. A number of other cases were seen but not treated, and a few were treated whose later careers were so incompletely recorded that they were of no value as evidence. I shall report today the result of our experiences with these 24 cases.

Very few cases of early carcinoma of the bladder come to the Huntington Hospital. Of the 24 cases in our series, 8 were cases of

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recurrence after operative removal of a carcinoma; 5 had been operated upon and a growth had been found which was too extensive for removal; 2 appeared after operations for stricture of the urethra; 9 were judged by cystoscopy to be unsuitable for any operation save perhaps the purely palliative procedures of cystostomy and cauterization. There were no benign papillomata in this series, and only one case in which excision of the growth might have been attempted with any success.

Speaking broadly, two types of treatment were used. The earlier method consisted in the application of screened radium emanation to the interior of the bladder, an attempt being made to apply the radium as closely as possible to the region of the tumor. For this purpose, the emanation, in its glass tube, was put into a thin steel needle, and then into a silver capsule with walls 0.5 millimeter thick, carried on the end of an intra-uterine applicator. The shaft of this was pliable and could be bent in such a way that the capsule at the tip could be applied fairly accurately to that quadrant of the bladder which contained the growth. In other cases, the radium emanation, in a steel needle, in some cases further screened by 0.5 or 1.0 millimeter silver, was placed in the tip of a soft rubber catheter. The catheter was inserted into the bladder and the patient instructed to lie in such position that the catheter would fall toward the affected part of the bladder.

The method which was employed in later case was the implantation of bare emanation tubes or of steel needles directly into the tumor.

It was first of all necessary to establish a standard dosage, to find, in other words, the number of millicurie hours which might be expected to cause retrogression of the growth, but which would not burn too severely the normal tissues of the bladder. From a series of cases as small as ours, treated by different methods over a term of years, it is difficult to cull the definite information which we would wish upon this point. Furthermore, there appear to be individual variations in the degree of reaction set up in different individuals by the same dosage. The amount of treatment which has already been given, the degree of cystitis, the type of tumor, the mechanical conditions of drainage (whether the urine has to be voided, is drained off suprapubically, or is excluded altogether from the bladder), all these factors influence the action of radium upon the bladder. The amount of screening is, of course, of importance.

I will give a few observations and try to ascertain from them the general limits of dosage.

Case 3 (Tothill). Woman, age 62, had an extensive carcinoma of the left lateral wall and base of the bladder. The growth was sessile and not ulcerated. Eighty-eight millicuries of radium emanation, screened by 2 millimeters silver, was placed in the tip of a soft rubber catheter and left in the bladder for 5 hours, 36 minutes. Total exposure 492 millicurie hours. She remained in the hospital 9 days after the treatment. Her temperature remained normal, and the only evidence of reaction was an increased frequency of urination at night.

Case 15 (Risnick). Woman, age 66, had a sessile, slightly ulcerated growth on trigone. Patient had had several treatments, the last one having been on February 12. April 20 she had no symptoms referable to the bladder. She was given a treatment, 66 millicuries of emanation, screened by 2 millimeters silver, applied to bladder base by means of intra-uterine applicator. The position of the applicator was changed once during the time—4 hours, 34 minutes—it was in the bladder. Total dosage, 300 millicurie hours. During the next 3 months, the patient showed no signs of radium burns. Cystoscopy, May 20, showed no burn of normal mucosa but did show retrogression of the tumor.

Case 18 (Robertson). Man, age 50. March 9, 1920. Cystoscopy; on left side of neck of bladder, extending for 1.5 inches above the internal urethral orifice and covering entire left half of bladder neck, is a massive, solid growth, necrotic in places. March 11, 100 millicuries, screened by 0.5 millimeter silver, screwed on to the tip of an intra-uterine applicator, were applied to the tumor for 3 hours. It was rotated once; dosage 300 millicurie hours. April: Since last treatment patient has had no haematuria or difficulty in voiding, nocturia four times, has gained 3 pounds. A cystoscopic examination was made and the bladder found not burned. The tumor showed reaction as evidenced by redness and oedema. April 15: cystoscopic examination was made and tumor seemed more extensive. Radium treatment, 66 millicuries, applied as before, for 4½ hours. Dosage 300 millicurie hours. May 20: patient has gained 10 pounds; urinates every 1 to 1½ hours; cystoscopy showed shaggy growth all around bladder neck, extending across trigone on to both lateral walls.

Another case (No. 19) developed considerable bladder irritation after 495 millicurie hours, with 1 millimeter silver and 1½ millimeters rubber screening.

Case 21 showed no reaction after 275 millicurie hours, with 0.5 millimeter silver screening.

Case 22. Woman with a recurrent carcinoma at the bladder neck, had a period of marked bladder irritability after 95 millicuries, screened by 0.5 millimeter silver and a rubber catheter, had been left in the urethra for 2 hours and 5 minutes (200 millicurie hours).

In two cases in which the urine was excluded from the bladder entirely, large doses of radium were applied intravesically. Case 14 had 1,000 millicurie hours with 0.5 millimeter silver screening. Case 20 had 1,008 millicurie hours, with no screening except that of a rubber catheter, inserted into bladder through the suprapubic sinus. Although in both cases the discharge of pus after radiation was annoying, in neither case was there pain in the bladder or any other subjective symptom due to the radium.

From a study of all our cases, of which the preceding instances are fairly typical, it would appear that 400 millicurie hours, given with a screening of 0.5 millimeter or 1.0 millimeter silver, is a dosage which may be used in the treatment of bladder cancer without any very marked reaction. Large doses in bladders which are subject to the alternate diastole and systole of urination, are likely to set up a reaction which is very painful. If the bladder is drained suprapubically, greater doses may be used, and if the urine is entirely excluded from the bladder, doses of 1,000 millicurie hours do not cause discomfort.

The duration of a reaction of moderate severity is from 4 to 6 weeks. Repeating the treatment in less than 6 weeks gives, therefore, cumulative effect. If, however, no reaction has developed in 3 weeks after the first treatment, it is proper to go ahead with the second treatment.

I have found that hæmorrhage and cystitis often decrease after a single radium treatment.

So much for the technical aspect of dosage. The question now arises: What is the effect of repeated or of single doses upon the cancer? Is the application of screened radium emanation to the surface of the tumor an effective method of treatment?

In our series 15 cases were treated in this way. Six had a total of less than 600 millicurie hours, 9 had 600 or more. I will briefly summarize these 9.

Case 1 (Wilde). September, 1916. Woman. age 60. August 1916, she had cystostomy by Dr. L. Davis. In the base of the bladder, easily palpable by vagina, was an infiltrating growth, the size of a silver dollar. Through the suprapubic fistula she was given 6 treatments, aggregating 1,900 millicurie hours, with screening varying from only that of the steel needle in which the glass emanation tube was contained, up to 1 millimeter silver. She was given 280 millicurie hours more by vagina. Five months after beginning this

treatment she died. Autopsy showed a sloughing, necrotic bladder, the wall of which contained carcinoma. There were metastases in the abdominal lymphatics and liver. There was a retroperitoneal abscess, a right perirenal abscess, a right pyo-ureter and pyelitis, left hydro-ureter and hydronephrosis. The carcinoma was not destroyed even locally after 2,180 millicurie hours.

Case 2 (Magnitzky). Woman, age 67, operated upon by Dr. Horace Binney, April, 1916. In October, 1916, she came to the hospital with recurrent carcinoma of the bladder neck. The base of the bladder was indurated over its entire vaginal aspect. She was given 3 intravesical treatments, totalling 848 millicurie hours, with 0.5 millimeter silver screening, and was given 696 millicurie hours over the lower abdomen. She died of carcinoma of the bladder in June, 1917. No autopsy. This was an evidently hopeless case apparently unaffected by radium.

Case 8 (Ligotte). Man, age 82. July, 1917, cystotomy was done by Dr. Paul Thorndike. Extensive carcinoma of base of bladder was found, and a suprapubic fistula established. In January and February, 1918, he was given two treatments aggregating 1,287 millicurie hours. Steel needles, unscreened, were inserted into the bladder through the fistula. Death from cancer of bladder occurred in September, 1918. This was an advanced case which was unaffected by radium.

Case 9 (Martin). Man, age 47, who, on December 1, 1917, had a cystotomy by Dr. W. C. Quinby. An extensive growth involving the trigone and left lateral wall of the bladder was found, and suprapubic drainage instituted. Beginning January 19, 1918, the patient had 6 treatments, extending over a period of 8 months. Steel needles containing radium emanation were put into the bladder through his suprapubic tube. A total dosage of 1,785 millicurie hours was given. At no time was there evidence of untoward reaction. Patient died at his home on December 19, 1918.

Case 11 (French). Man, age 66. November 6, 1917; operation by Dr. G. G. Smith. A malignant growth near right ureter excised, and a rough area on anterior commissure cauterized. Pathological report: cancer. On February 14, 1918, cystoscopy showed an area of rough appearance on anterior commissure, which suggests cancer. March 2, 1918, 204 millicuries, screened only by steel needle and rubber catheter inserted so as to lie just inside bladder orifice. Left in for 3 hours, total 612 millicurie hours. Patient was not seen again, but telephoned that he was having a great deal of bladder trouble. Died July 3, 1918. No autopsy. A case of localized malignant growth of bladder neck, treated once. In this case 612 millicurie hours proved ineffective in checking growth.

Case 14 (MacBeth). Man, age 61. Bladder full of shaggy growth. Operation, December 3, 1919. Dr. G. G. Smith. Five papillomatous growths were removed, bases cauterized, no apparent induration of bladder wall. Two bare emanation tubes of 8 and 6 millicuries respectively buried in cauterized area outside of right ureter. These total 1,864 millicurie hours. Specimen showed carcinoma. March 18, 1920, cystoscopy; bladder wall smooth except for a necrotic area, 2 centimeters in diameter, surrounded by a zone of heaped up, deep red tissue, outside of right ureter. Given radium treatment, 150 millicurie hours, screening 1 millimeter silver and rubber catheter. May 6, he was given 219 millicurie hours, screened by 0.5 millimeter silver. June 3 he was given 300 millicurie hours, screened by 0.5 millimeter silver. August 28, his symptoms of bladder irritability were worse, and cystoscopy showed papillary masses of necrotic tissue rising from the right lateral wall. His tumor had grown, although he had had 669 millicurie hours radium besides the 1,864 millicurie hours introduced at operation. The neck of the bladder was red and oedematous, evidently a reaction to the radium. A bilateral ureterocolostomy was done in October, 1920. He did well and was given 1,000 millicurie hours, 0.5 millimeter screening, intravesically on November 24, 1920. He then went home to Providence, but a letter received March 12 stated that he was suffering greatly from pain in back and legs and was too ill to be brought to the hospital.

Case 15 (Resnick). Woman, age 66. January 3, 1920. Cystoscopy showed the base of the bladder from above the ureters to the urethral orifice to be covered with a sessile, irregular, non-ulcerated growth. Palpation of base of bladder detects several smooth, firm nodules, the size of beans in the vesicovaginal septum. January 7: 2 bare emanation tubes of 3 millicurie each were inserted into the largest nodules through an endoscope. January

29: bleeding stopped; there is more frequency of urination and some ardor urinae; cystoscopy shows no appreciable change; 1,155 millicurie hours, screened by 2 millimeters lead applied to base of bladder by vagina. February 11: 730 millicurie hours, screened by 2 millimeters lead, applied by vagina. February 12: 276 millicurie hours, screened by 1 millimeter silver, applied intravesically by means of intra-uterine applicator. March 18: no symptoms now; cystoscopy showed trigone free from growth except for 1 nodule, size of cherry, near right ureter. This mass is palpable by vagina. Close to bladder neck, on right, the mucosa is thickened. April 15: cystoscopy showed on right side of trigone an elevated mass about 1 inch in diameter, with necrotic areas. April 20: 300 millicurie hours screened by 1 millimeter silver introduced into bladder on intra-uterine applicator. May 20: cystoscopy showed 2 nodules near right ureter, small nodule near left; 400 millicurie hours applied by vagina, 2 millimeters lead screening. November 4, 1920: lately has had some frequency and haematuria. Cystoscopy showed 2 solid tumors, each about 1 centimeter in elevation and 2 or 3 centimeters in diameter. Some roughening of the mucosa on right side of trigone. November 30, 1920, cystotomy: a circular growth, 2 centimeters in diameter surrounding left ureter. Into this were inserted 3 bare tubes totalling 20 millicuries. To right of urethra a growth 2 by 0.5 centimeters, in to which were put 3 "seeds," aggregating 11 millicuries. Outside right ureter is a growth 3 by 2 centimeters, 1 centimeter high. This was leveled off with the cautery and into the base were inserted 3 seeds amounting to 22 millicuries. Thus a total dosage of 6,800 millicurie hours was given. The bladder was drained suprapubically for 3 weeks. During convalescence the patient had a good deal of bladder pain. She was discharged January 3, 1921. March 10, 1921: cystoscopy showed great masses of necrotic tissue about the base of the bladder. The ring of growth about the left ureter was gone, leaving a zone of necrosis. The patient was feeling fairly well and her condition was improving.

This case showed very definite improvement following screened radiation from bladder and from vagina. After an initial improvement the growth again became active and was treated by open operation and implantation of bare emanation tubes. Final result as yet unknown.

Case 18 (Robertson). A man of 50 had had haematuria for 2 years. March 6, 1920, cystoscopy: "On left side of bladder extending for 1 or 1½ inches above urethral orifice and occupying entire left side of bladder neck is a massive, solid growth, necrotic in places, apparently continuous with the prostate. Prostate by rectum feels small and soft."

March 11 he was given 300 millicurie hours, 0.5 millimeter silver screening. April 15 this was repeated. Cystoscopy; tumor seems more extensive. May 20: patient has been working and has gained 10 pounds; no haematuria; voids every hour or hour and a half. Cystoscopy: shaggy growth all about bladder neck, extending across trigone and on to both lateral walls. Ureterosigmoidostomy was done. The patient had postoperative intestinal obstruction. He was explored and a definite obstruction freed, but he died 5 days later. No autopsy could be obtained. 600 millicurie hours did not check the growth.

Case 19 (Boston). Man, age 52. April 12, 1920. Bladder appeared to be full of a shaggy growth. April 15: 495 millicurie hours radium emanation, screened by 1 millimeter silver, contained in soft rubber catheter. Position of the catheter was changed 3 times during the treatment. May 13: has had considerable bladder reaction; now better. June 3, patient working on the road, urine less foul. Cystoscopy: 3 or 4 sloughing papillary growths on left lateral wall and on trigone. Somewhat less growth, less cystitis. June 17, has had to stop work because of bladder trouble. Given 243 millicurie hours, screened by 0.5 millimeter silver. July 8: passes pieces of slough. Base of bladder above prostate feels indurated; much frequency. Operation advised, but patient did not return. A letter states that he died in December, 1920, of cancer of bladder.

Case 24 (Belcher). Woman, age 76. Cystoscopy, June 9, 1920: trigone covered with necrotic growth. Another area back of left ureter. June 8: 91 millicuries, screened by 0.5 millimeter silver, left in bladder for 3.5 hours. Total 300 millicurie hours. July 1: symptoms improved. Cystoscopy: less slough, growth smaller. Ureters now visible. July 15: 99 millicuries radium, screened by 2 millimeters lead, applied to base of bladder from vaginal side

for 8 hours. August 19, cystoscopy: trigone apparently free of growth, a few small buds in right base; 152 millicuries, screened by 0.5 millimeter silver, applied to right base of bladder on intra-uterine applicator, for 2 hours. October 7: can hold urine for 2 hours, urine clear. One necrotic papilloma near right ureter. A few buds in right base. October 21: a necrotic growth 2 centimeters in diameter near right ureter. Masses of slough about the bladder neck. November 18: 126 millicuries, screened by 2 millimeters lead, applied by vagina for 4 hours. December 7, growth is increasing, has had 1,900 millicurie hours. December 21, cystotomy: ulcerated area about bladder neck and on trigone. A bit excised. Pathological report: necrosis and inflammatory changes. Some small arteries containing organized thrombi; no carcinoma.

Three bare emanation tubes of 3 millicuries each were inserted—1,200 millicurie hours. Three needles aggregating 44.5 millicuries were left in the tissues about the bladder neck for 24 hours—1,078 millicurie hours. The patient lived for 6 weeks, gradually failing. Autopsy: "Annie Belcher: microscopic notes. None of the numerous sections through the wall of the urinary bladder and neighboring tissue shows carcinoma. There is an acute purulent cystitis, ureteris (bilateral), and inflammation (acute pyonephrosis) of the kidneys. Lymph-glands show acute inflammation. The bladder wall is considerably thickened by an increase of dense fibrous tissue between the muscle bundles, indicative of long-standing chronic cystitis.

It may have been that in this case the carcinoma had been already destroyed by radium before operation. As a result of two treatments—800 millicurie hours within the bladder, 800 millicurie hours by vagina—a fairly extensive and certainly inoperable growth was almost entirely cleaned up. It began to grow again, however, and increased in spite of 300 millicurie hours intravesically and 500 millicurie hours vaginally.

Of the 6 cases treated with less than 600 millicurie hours, none showed improvement worth noting. Of the 15 cases treated by screened radium emanation inserted into the bladder, only 3 showed any marked improvement. This improvement, in Case 19, lasted about 1 month; in Case 15 it persisted for 7 months at least; in Case 24 the cancer may have been destroyed before cystotomy.

The use of screened radium emanation introduced into the vesical cavity, while not wholly ineffectual, was far from encouraging. Although in some cases the amount of treatment was undoubtedly too small, the cases given treatment to the point of burning the bladder were sufficient in number to convince us that a more intimate aplication of the radium to the tumor was desirable. In our later cases we have, therefore, tried to get the radium directly into the tumor. In 3 cases this was done without opening the bladder; in 3 it was done by cystotomy.

Case 15 has already been described. Two "seeds" were inserted through the endoscope; the number of seeds was inadequate to the size of the growth.

Case 17 (Kettleman). Man, age 67. Cystoscopy, February 17, 1920, showed a large adenomatous prostate. On the anterior vesical wall just behind the anterior commissure of the prostate was a partly necrotic, sessile tumor, about 2 centimeters in diameter. March 3, with cystoscope in the bladder, a long needle bearing in the tip 68 millicuries of radium emanation was inserted through the space of Retzius until the tip could be seen issuing from the tumor. It was then withdrawn slightly and left in position for 3 hours. (Total 204 millicurie hours). March 18, the tumor had almost disappeared. May 13: no sign of the tumor. I could not see the bladder wall close behind the prostate, so by means of an intra-uterine applicator I applied 138 millicuries, screened by 2 millimeters silver, to the anterior bladder wall for 1 hour, 30 minutes (200 millicurie hours). March 10, 1920: the patient re-

turned for examination. He had gained weight and looked well. He had no bladder symptoms. Cystoscopy showed no sign of tumor in the bladder.

Case 22 (Mrs. Quinn). Woman, age 28, from whose bladder a papillomatous growth the size of a horse-chestnut had been removed at the Boston City Hospital. The operation was on February 28, 1919. June 24, 1920, haematuria reappeared. Cystoscopy, July 22, showed a solid, rounded tumor, the size of a marble, rising from right bladder neck. A needle containing 125 millicuries radium emanation was passed through the vesicovaginal septum into the tumor and left for 4 hours—(500 millicurie hours.) August 19: tumor reduced one-half; 424 millicurie hours applied by vagina. October 21: endoscopy gives good view of a tumor, size of pea, close to internal orifice. Through the endoscope a needle bearing 28 millicuries was inserted into the tumor, and left for 8 hours (224 millicurie hours). December 2: tumor is gone, white slough at neck of bladder. Patient is 2 months pregnant. February 3, 1921: no growth seen, considerable slough about bladder neck. Patient has had a severe attack of cystitis. February 10, 1921: 95 millicuries, screened by 0.5 millimeter silver, placed in catheter and left in bladder neck for 2 hours, 5 minutes (200 millicurie hours). March 5: patient is having a good deal of bladder distress.

The three cases in which bare tubes were implanted by cystotomy have already been described.

Case 14 had two seeds of 8 and 6 millicuries (1,862 millicurie hours) implanted and 8 months later showed a definite recurrence.

Case 15 had seeds totaling 53 millicuries (7,049 millicurie hours) implanted on November 30, 1920, and 3½ months later showed a great mass of necrotic tissue in the regions so treated. Whether there is still cancer present, cannot yet be told.

Case 24 had seeds and needles implanted totaling 2,278 millicurie hours. At autopsy 6 weeks later no carcinoma could be found.

I am painfully aware of the incompleteness of this series of cases. In many the diagnosis was never made microscopically, although in practically all the diagnosis was made by several cystoscopists. There were but few autopsies upon the cases that died, and as for the few patients still alive, sufficient time has not elapsed to prove the value of this treatment. Certain conclusions, however, have formulated themselves in my mind, to form a starting point for further work.

Conclusions 1. It is useless to attempt to cure with radium infiltrating carcinomata which involve large portions of the bladder wall. Necrosis of the bladder will be brought about by any dosage which will materially influence the tumor.

2. Certain superficial cancers of the bladder may be reduced in extent by the application of screened radium emanation to their surface. This may occur without necrosis of bladder wall.

3. To accomplish this effect, 400 millicurie hours, with screening of 0.5 millimeter silver, applied not oftener than once in 6 weeks, has been successful, and has not caused any considerable reaction in the bladder.

4. The greatest effect is produced by the first 3 or 4 applications of radium.

5. If the tumor begins to grow again, further treatment with radium applications has little deterrent effect.

6. The best way to employ radium in cancer of the bladder is by

the implantation of bare emanation tubes in the tumor, allowing one tube to each cubic centimeter. Steel needles containing radium may be employed in the same way, except that they must be withdrawn after adequate exposure has been made.

7. The necrosis caused by the implantation of radium in bladder tumors persists for at least 3 months.

REVIEWS AND ABSTRACTS.

Douglas Quick, M. D., New York City. (Attending Surgeon, Memorial Hospital). The Treatment of Cancer of the Rectum by Radium. Am. J. of Roentgenology, viii, 746-753, Dec., 1921.

"In reviewing our work of the past few years in rectal cancer it would be useless to attempt a statistical report, for various reasons. Most of the cases treated have been far advanced in the course of the disease and, while valuable information has been obtained from the radium standpoint, the most that could be hoped for from the patient's side was a certain degree of palliation. The lapse of time over which statistics become of real value has not been great enough."

"We are stimulated by the surgical results to date to look for another method of treating rectal cancer and our experience with radium encourages us in proceeding along the present lines."
knowledge of their response to radium from experience with the same types of growths in other parts of the body. The problem is therefore largely one of technique. Unfortunately this is not as simple as it might seem."

"We have treated in all 161 cases of rectal cancer at the Memorial Hospital during the past four years. Of these practically all were very advanced cases: many hopelessly disseminated, others advanced recurrences."

"A large number of cases have been benefitted from one to three years and then died of distant involvement or some intercurrent disease; others are still improving, and some with a fair hope of complete regression of the disease, providing there is not already distant metastasis. By improvement I mean inhibition of the growth, very frequently decrease in its size, with fibrosis which tends to create a local process rather than an actively growing disseminating one. The decrease in size relieves the partial obstruction; constipation is therefore less marked. Bleeding is largely stopped, discharge of mucous is lessened and pain is very materially decreased."

"Fourteen patients only out of the entire series are now clinically free from disease for periods ranging from four months to four years. Two of these cases were granulomas of the type of lymphosarcomas while the others were typical adenocarcinomas or epidermoid carcinomas. The oldest case now free from disease for about four years has a marked fibrous tissue stenosis due to over-radiation with heavily filtered radium placed within the lumen of the gut. This error we feel we can now safely eliminate by proper protection."

"During the past year we have been impressed by the number of

cases that seemed to improve for a short time and then distant metastases, usually in the liver, became evident. Under such circumstances it is quite evident that the initial discomfort resulting from intense radiation of the local lesion is not warranted if the disease has already become generalized. In view of this we now feel that an exploratory laparotomy is justified in most instances where the local growth presents possibilities of complete regression from the use of radium."

"We have not done a colostomy as a routine procedure. * * * * I would urge a colostomy only in the case where radium application would be facilitated by it and where the possibilities of closing it after treatment were good. In impending obstruction it is of course imperative. In the large group of advanced cases who can control bowel function fairly well we leave the decision to the patient."

"At first we used only one tube of 1 mm. platinum filter in rubber inserted into the stricture or packed against the lesion with gauze where the growth did not involve the entire circumference of the gut. Following this we used tubes of the same filtration but arranged end to end in tandem fashion, enough to extend beyond the limits of the growth above and below. These were inserted in a small rubber tube inside a larger rubber rectal tube to afford some distance, because we soon learned that the rectal mucosa did not stand radiation nearly as well as the mucous membrane in other parts of the body. This factor of irritation of normal rectal mucosa has rendered the treatment of cancer in this location much more difficult than it otherwise would be."

"In 1917, we began using radium emanation interstitially and in a previous publication Janeway has mentioned its use in connection with rectal cancer. This method has added more to our improvement in results than all other changes combined. It permits of distributing the radiation throughout the growth so that an accurate approximation can be made. It permits of using both the beta and the gamma radiation thus resulting in a saving of radium energy. It can be introduced into the upper portion of a growth through an abdominal incision and left in situ. It permits of a continuous radiation over a period of a few weeks thus resulting in greater dosage being possible than where filtered tubes or needles containing radium element are inserted for a few hours and than withdrawn. These emanation tubes may be inserted, by means of the usual trocar needles, through the proctoscope or as I frequently prefer, if the growth be low down, through a small cannula which is inserted alongside the examining finger. Palpation is always more important than direct vision in inserting radium emanation tubes. The tubes are about 3 mm. in length and 0.3 mm. in diameter and so far we have observed no ill effects from them as foreign bodies. In our earlier work we used tubes of too great strength but now we have reduced the strength of individual tubes and can thereby get a more uniform distribution by using a greater number of tubes. At present we are using tubes of about 1 mc. although in some very bulky growths it is quite safe to use tubes up to 2 mc. in strength. One mc. of radium emanation left in situ until exhausted gives a total radiation of approximately 132 mc. hrs. Depending upon the size and distribution of the growth our dosage of buried emanation varies from 10 to 40 mc. or a total of 1320 to 5280 mc. hrs."

"It is frequently possible to introduce these tubes into the rectal tumor without anesthesia because the pain is very slight but I am in

favor of a short gas and oxygen anesthesia in most instances. The relaxation by the anesthetic permits of a more accurate distribution of the tubes."

"With the early use of buried emanation we fell off very sharply in the use of filtered radium internally. We soon found that this was a neglect of opportunity to get in an appreciable quantity of radiation at close range, and have resumed its use. Where the growth is annular a string of ½ mm. platinum tubes, usually 3 to 5, arranged end to end in a small rubber tube which is again encased in a larger rubber rectal tube with a metal end to facilitate introduction, is placed within the stricture. They may be inserted directly or through the proctoscope. A sufficient number of tubes should be used to go beyond the limits of the growth both above and below. Using this filtration and protection a dosage of 500 mc. hrs. per tube does not give an undue reaction. Where the growth is limited to one segment of the rectal wall a slightly different type of applicator is employed. Solid rubber rectal bougies of various sizes with two grooves cut in the side are employed. In these grooves the required number of platinum tubes in small rubber tubes are placed. Knowing the axis of the growth and its distance from the sphincter it is possible to insert this applicator so that the tubes come in accurate and close approximation to the growth. If necessary it may be rotated in order to complete the application. This applicator has the advantage of protecting by distance the opposite uninvolved rectal mucosa from the full dose of radium used over the growth. We now feel that it is a distinct advantage to use an internal dose of filtered radium before burying emanation tubes throughout the growth. The surface radiation applied in this way inhibits the growth and produces at least a temporary retrograde process during the course of which it is safer to introduce the needles carrying emanation tubes. The theoretical danger of dissemination by trauma is thereby obviated or materially lessened."

"Carcinoma low down in the female rectum offers a more favorable opportunity for treatment because it can be reached through the posterior vaginal wall. For this purpose we use small 2 mm. lead or brass plaques of about 4 sq. cm. surface area as the filtering applicator. One, two, or three of them depending on the individual requirements may be placed over the posterior vaginal wall and the other walls packed away with gauze packing. It is best to separate the plaques about 1 cm. from the posterior vaginal wall and at this distance 800 mc. hrs. per plaque with the lead or slightly less with the brass, can be given with safety in addition to that already used within the rectum. This adjunct is of most value of course where the growth is low down and involving the anterior rectal wall."

"At first we were disposed to apply all of our treatment from within but more recently we have been convinced that it is necessary to attack rectal cancer from every available angle if we are to hope for complete regression of the disease with any degree of uniformity. We have therefore resorted to heavily filtered doses of radium applied at a distance from the skin over the sacrum and, if the growth be higher up, through the left lower quadrant as well. For this purpose our usual 70 sq. cm. radium pack is used. This pack is filtered by 2 mm. of brass, and at a distance of 10 cm. from the skin 20,000 mc. hrs. of radiation can be given with safety. We feel that this adds very materially to the ultimate result."

"While our dosage has always been directed toward giving as much as possible with a given applicator, our technique, it will be seen, has changed very materially in the past year. We feel that with this effort to deliver as much radiation from as many avenues of approach as possible in the cases for whom we hold out a possibility of complete regression, our results have been much more encouraging."

"Every case of rectal cancer presenting for treatment should be classified in one of three groups depending on extent of primary growth, metastases or probability of metastases, age and general physical condition."

"Group 1. All cases for whom a reasonable hope for complete regression can be entertained.

"Group 2. Advanced cases for whom a reasonable hope for palliative relief can be entertained."

"Group 3. Hopelessly advanced cases for whom the physical agents hold out no chance for relief."

"In Group 2 we should give first consideration to the comfort of the patient throughout. If surface applications of radium internally will relieve discharge, bleeding, pain and obstruction and prolong life then it should be employed with that end in view but not pushed to the point of serious discomfort. I believe that in these cases buried emanation should be used sparingly, if at all."

"In Group 1 we should make use of radium in as large doses as possible and through all available channels to effect a complete regression. In the majority of these cases I am convinced that an exploratory laparotomy is advisable."

"We feel, however, that our experience throughout this period of evolution in technique and methods of radium application warrants us in treating the operable as well as some of the more advanced cases, with a reasonable hope for success."

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